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BULLETIN OF THE HISTORY OF MEDICINE

ORGAN OF THE AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE AND THE JOHNS HOPKINS INSTITUTE OF THE HISTORY OF MEDICINE

Editor—HENRY E. SIGERIST

Associate Editor—GENEVIEVE MILLER Medical Library

VOLUME XVI DECEMBER, 1944 NUMBER 5

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THE JOHNS HOPKINS PRESS

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Correspondence relating to the publication of papers should be addressed to The Editor, Bulletin of the History of Medicine, 1900 East Monument Street, Baltimore—5, Maryland, U. S. A.

Twenty-five reprints without covers will be furnished to contributors free of cost. An order slip for additional reprints, giving the cost, is sent with the galley proof to each contributor and must be returned immediately to the Editor.

The journal is published monthly, except August and September. Two volumes of at least 500 pages each are published during the year.

Subscription is $5.00 a year in the United States and its possessions; in Canada $5.75 a year; in foreign countries $5.50 a year. Single numbers, when available, will be 75 cents each. Members of the American Association of the History of Medicine receive the Bulletin on payment of $5.00 annual dues, of which $4.00 is for a year's subscription to the Bulletin.

This journal will publish book reviews, and publishers are requested to send review copies to the Editor.

Back numbers of Volumes II to VIII of the Bulletin of the History of Medicine are available through the Johns Hopkins Press for $5.00 a volume, of Volumes IX to XV for $2.50 each. Volume I is out of print.

Supplements to the Bulletin are published at irregular intervals and are sold individually, whereby subscribers to the Bulletin are granted a reduction of price. Standing orders for the whole series of Supplements may be addressed to

THE JOHNS HOPKINS PRESS

BALTIMORE 18, MARYLAND, U. S. A.

A MONTHLY EXCEPT AUGUST AND SEPTEMBER

Made in United States of America

Entered as second-class matter January 3, 1935, at the post office at Baltimore, Maryland, under the Act of March 3, 1879.

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AN EIGHTEENTH CENTURY PLAN FOR A NATIONAL HEALTH SERVICE

GEORGE ROSEN

Characteristic of England during the later 17th and early 18th centuries is the creation of elaborate plans for commercial undertakings, technological innovations, and social reforms, in short, the making of projects. This tendency is perhaps best described in the words of Daniel Defoe. "Necessity, which is allowed to be the mother of invention," he wrote in 1697, "has so violently agitated the wits of men at this time, that it seems not at all improper, by way of distinction, to call it the Projecting Age. For though in times of war and public confusions the like humour of invention has seemed to stir, yet, without being partial to the present, it is, I think, no injury to say the past ages have never come up to the degree of projecting and inventing, as it refers to matters of negoce and methods of civil polity, which we see this age arrived to." [1]

One of the most interesting and at the same time one of the least known of these projects is the proposal of John Bellers for the establishment of a national health service. The name of John Bellers is not to be found in histories of medicine; it is better known to the student of economic and social history.[2] Yet the name of a man who was a pioneer

[1] Daniel Defoe: *An Essay Upon Projects*, London, 1697, in: *The Earlier Life and The Chief Earlier Works of Daniel Defoe*, edited by Henry Morley, London, George Routledge and Sons, 1889, p. 31. See also Werner Sombart: *Der Bourgeois, Zur Geistesgeschichte des modernen Wirtschaftsmenschen*, München and Leipzig, Duncker & Humblot, 1920, pp. 54-55, 66-67.

[2] Marx referred to Bellers as "a phenomenal figure in the history of political

in a field such as the provision of medical care, which assumes ever increasing significance with each passing day, certainly deserves a better fate at the hands of the medical historian. It is the purpose of this paper to present the proposal of Bellers and thus to draw attention to his significant contribution. I make no claim of priority for Bellers in this field. Indeed, it appears likely that he had been preceded in some degree by earlier writers. For example, John Cook in his *Unum necessarium* (1648) had pleaded for the relief of the poor, including free medical service.[3] The plan put forth by Bellers, however, is elaborately worked out and contains a number of features of particular interest.

John Bellers (1654-1725) was a Quaker cloth merchant of London who around 1679 began to carry on philanthropic work.[4] It seems likely that this work started him on his projects for improving the lives of the poor. To this end he put forward a number of proposals verbally and in books. The best known of these writings is his *Proposals for Raising a Colledge of Industry of all useful Trades and Husbandry, with Profit for the RICH, a Plentiful Living for the POOR, and a Good Education for YOUTH. Which will be Advantage to the Government, by the Increase of the People, and their Riches*, London, 1695. This was a plan for the creation of Colleges of Industry that would furnish employment for poor people. In 1710 he published *Some REASONS* for an *EUROPEAN STATE, proposed to the Powers of Europe. By an Universal Guarantee, and an Annual Congress, Senate, Dyet or Parliament. To Settle any Disputes about the Bounds and Rights of Princes and States hereafter. With an Abstract of a Scheme form'd by King Henry the Fourth of France upon the same subject*, etc., London. In this work Bellers presents in essence a plan for a League of Nations.

In 1714 Bellers published a treatise in which he set forth a plan for a national health service. This is the substance of his *ESSAY Towards the IMPROVEMENT of PHYSICK. In Twelve PROPOSALS. By which the LIVES of many Thousands of the Rich, as well as of the Poor, may be SAVED Yearly. With an Essay for Imploying the Able POOR, by which the Riches of the Kingdom may be greatly Increased;*

economy "; see *Capital*, trans. by Eden and Cedar Paul, Everyman's Library Edition, 1930, vol. 1, p. 527.

[3] A. S. P. Woodhouse (editor): *Puritanism and Liberty, Being the Army Debates (1647-9) from the Clarke Manuscripts*, London, J. M. Dent and Sons, Limited, 1938, p. 48.

[4] A. Ruth Fry: *John Bellers, 1654-1725, Quaker, Economist and Social Reformer. His Writings Reprinted, With A Memoir*, London, Cassell and Company, Ltd., 1935, pp. 5-28.

Humbly DEDICATED to THE PARLIAMENT of Great Britain. The book consists of 11 sections as follows.

1. To the Parliament,
2. Twelve Proposals for the improvement of Physick,
3. Reasons for to Support those Proposals,
4. To the Physicians of Great Britain,
5. An Essay on Health, Sickness and Medicine,
6. To the Lord Mayor, Aldermen and Common Council of the City of London,
7. To the Governors, Directors, &c. of the South-Sea-Company,
8. Proposals for a Profitable Imployment of the Poor,
9. A Summary of the foregoing Discourses,
10. Several Objections Answered,
11. A Postscript to the Men of Wit and Pleasure.

Of these, sections 2-3 are devoted to the problems of medical service, while the others appeal for support of his plan and recapitulate Bellers' proposals for improving the condition of the poor, in particular his plan for a College of Industry.

Bellers begins by addressing himself " To the Lords and Commons of Great Britain, in Parliament assembled." Pointing out the great importance of disease and ill health, he suggests the need for consideration of this problem by the government. By way of illustrating the magnitude of the problem, he says: " There are twenty thousand or more, who die yearly, within the bills of mortality of London and Westminster, in which compass, it is supposed that there are about a tenth part of the people of South Britain only; and therefore, it may well be computed, that there are about two hundred thousand who die within the kingdom in the same time; though we have no pestilencial distemper rages among us, but our animosities.

" And it may be reasonably supposed, that a hundred thousand of those two hundred thousand, die yearly of curable diseases; for want of timely advice, and suitable medicines.

" Considering that above three quarters of our people are poor, and not able to procure either, but what's of charity; and therefore many of them must be lost, and die miserably, for want of a suitable provision for them. Besides, in time of contagion, their poverty makes them the more liable to infection; as is supposed, was their case, lately in Swedeland." [5]

[5] John Bellers: *An essay towards the improvement of physick, in twelve proposals, by which the lives of many thousands of the rich, as well as the poor may be saved yearly . . .*, London, J. Sowle, 1714. The address to Parliament comprises pages 1-6.

But, continues Bellers, even those who can command medical attendance, also have an interest in the improvement of medicine. For as physicians learn more about disease the well-to-do will also benefit from this knowledge. "And if the other part of our people," he says, "can procure a physician's attendance, yet diseases and medicines are so mysterious in many cases, and of those which are known by some physicians, are but so little understood by many others that it may be questioned, whether one half of the rich may not die of such maladies as would be curable, if diseases and medicines were bettter understood, and more universal.

"And who knows whether himself, a favourite daughter, or his only son, the heir and hopes of his family, may not be of that number?"

Bellers was aware that a certain mortality is indicative of an even greater morbidity. "If a hunderd thousand of our people," he writes, "fall yearly by untimely deaths, it may be supposed that there are a million sick in a year, among us, of whom many are very deplorable cases." Consequently, it is necessary to take action to improve the state of medicine. Provision of this nature will undoubtedly have salutary social and economic effects. "Wherefore," Bellers continues, "*If the safety of the people be the supreme law*, we have then but few articles in our statute book of so great a consequence, as such an Act of Parliament will be, that shall make a thorough provision for the improvement of medicine."

Bellers realized that there was a good deal of unnecessary illness, and also that such sickness and the resulting deaths represented an appreciable economic loss to the community. "Every able industrious laborer," he points out, "that is capable to have children, who so untimely dies, may be accounted two hundred pound loss to the kingdom." [6]

[6] *Ibid.*, p. 3. It is worth noting that this is one of the earliest attempts if not the earliest, to assess the economic loss to society resulting from unnecessary mortality. This aspect was touched on and developed by a number of later writers of whom we can mention only a few: Josiah Curtis, *Brief Remarks on the Hygiene of Massachusetts, but more particularly of the cities of Boston and Lowell: Being a Report to the American Medical Association* etc., Philadelphia, 1849 (Curtis quotes a number of English authors on the money loss sustained through avoidable illness); J. C. Simonds: *The Sanitary Condition of New Orleans, as Illustrated by its Mortuary Statistics*, Charleston Med. J. and Review, 6: 677-745, 1851 (Cf. H. E. Sigerist, The Cost of Illness to the City of New Orleans in 1850, *Bulletin of the History of Medicine*, 15, 498-507, 1944); John H. Griscom: *Sanitary Legislation, Past and Future: The Value of Sanitary Reform and The True Principles For Its Attainment. Parts of Two Essays Read Before The New York Sanitary Association, October 3rd and November 14th, 1861*, New York, 1861, pp. 17-22; William Farr: *Economic Value of Population*, in *Vital Statistics*, London, 1885, pp. 59-64; Max von Pettenkofer: *The Value of Health to a City, Two Lectures De-*

But any program to implement such a legislative enactment must be carried on in large part by the government, as " it is too great a burden to be left upon the shoulders, or to the care of the physicians alone, no private purse being able to bear the needful charges of it. Especially considering the necessity of many and the indifferency of others of that faculty, further than to procure a plentiful substance for themselves: And how much it concerns every other person, there is the more reason to expect, the State should bear a good part of the expense of it."

After introducing his subject and pointing out the need for legislative action, Bellers presents his program for a national health service in the form of the following twelve proposals:

THE PROPOSALS[7]

1) That there should be built, at, or near London, hospitals for the poor; if not one hospital for every particular capital distemper; for the entertaining of such poor patients, whose conditions may want it: and to have physitians and chirurgeons suitable, to take care of the sick.

And that each patient be registered in a book, with the daily prescriptions that is made for them, and how they succeed.

And when any one dies in the hospital, their bodies should be opened, for the better information of the phisitians.

All which proceedings, should be ready to be seen by physitians, for the universal spreading of knowledge among the faculty, and good of the publick; that their advice may be the more effectual when any patient may want their assistance.

Which may prevent many from travelling to foreign hospitals to learn, when they shall be capable of doing it better at home.

II. That one hospital should be more particularly under the care and direction of the Queen's physitians; that they may take into it such patients, whose infirmities at any time, our sovereign may be subject to: In which hospital, her physitians may not only use what method, or medicines they apprehend may be most effectual in that case. But if any other physitians shall think they are capable of helping in such an illness, that they be allowed to take care each of one of the patients, and a register kept of their success.

Then the Queen's Physitians, will have the united opinion and experience of so many more of the faculty, as well as their own; by which they will be capable of

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livered in 1873. Translated from the German, with an Introduction by Henry E. Sigerist, Baltimore, The Johns Hopkins Press, 1941.

It is also worth noting that this approach is first enunciated by a Quaker merchant. This raises the question as to the degree to which it is a product of the rational, calculatory aspect of the Protestant ethic (see Max Weber: *Die protestantische Ethik und der Geist des Kapitalismus*, in: *Gesammelte Aufsätz sur Religionssoziologie*, vol. 1, Tübingen, 1922, pp. 17-207).

[7] Bellers, *An essay towards the improvement of physick . . . .* pp. 7-10.

prescribing for the Queen with the less hazard of mistaking: Experience making the best physitians.

III. That there be one hospital for the blind.

IV. That one hospital should be for the incurable, whom the physitians of any other hospital, shall have declared such.

And that any person may have the liberty to give medicines to such incurable patients, as are willing to follow the prescriptions.

And such as make any cure, should be rewarded by the state, if the patient is not able to do it.

And after many repeated cures of such patients, a gratuity should be given by the government, to the owner of such medicines, to make a public discovery of them.

And if he desires it, to be placed as a physitian, in one of the hospitals where his medicine is proper.

Which may be a means of preventing the loss of some good medicine.

V. That a public laboratory and a physical observatory be provided; not only to prepare all the chymical medicines now used in physick: but also, to make a general search among the vegitables and minerals &c. what further discoveries can be made, for to help the sick.

And that some be appointed to examine the temper and texture of all the fluids of the body; as well of the healthy, as of all the different diseased constitutions.

And of the uses of the several natural evacuations of the body, and what are the consequences of any one of them being obstructed, and the diseases which they produce.

VI. That there be one hospital at least, at each of our two universities; with different wards for each distemper.

VII. That in every hundred of a county, and parish of a city, there be appointed one doctor and chirurgeon (or more, if needful) to take care of the sick poor in them; who should visit every parish once a week, at least.

And they to be paid by the overseers of the poor: And such whose illness may be chronical, especially if declared to be incurable, they should be sent to the most suitable hospital.

VIII. That all medicines that are daily published as extraordinary, to invite patients, should be thoroughly examined, with the greatest candor and exactness that possible may be.

And that publick notice should be given of it, as the case requires, if a good medicine, that the owner may be encouraged, and the publick receive the benefit of it; and if a bad one, that the nation may be prevented from being cheated by it.

IX. That some physicians and chirurgeons should be sent into the East and West Indies, and the continent of America, to seek what may be found of useful medicines among the Indians and Negroes.

And all chirurgeons of ships should be directed to make what useful discoveries they can, in every country they come to, and that they have a suitable gratuity of the state for any that they shall make.

X. That the Colledge of Physicians, and Company of Chirurgeons, should draw up a summary of advice, in both their faculties, in the plainest manner, of what common errors should be avoided in practice, as well as what is fit to be done; for a general information to all practitioners in physick and chirurgery through the nation, that they may be the more successful to their patients.

And that there may be a committee appointed to attend at the Colledge of Physicians every post day, to correspond with the country physicians in case any of them should meet with a difficulty and they shall want advice upon it.

For which they should have an allowance by the state.

XI. That the Royal Society (founded by King Charles the II) have some endowment, the better to enable them to carry on that useful and great design, of improving men in the knowledge of nature (and the mechanicks) of which medicine is a principal branch.

And there should be a gratuity, or prize, allowed to such persons, who shall discover any thing new in nature, or the mechanicks.

XII. That both Houses of Parliament, should each please to appoint a committee every sessions, to enquire of, and receive from the Colledge of Physicians, an account of the state of medicine; and whether any new discovery hath been made for the improvement of it.

And if any other person hath any thing to offer on that subject, that they may be heard.

For as every new law hath a new evasion, there is the more need for our Legislature the oftener to see how well that law is put into practice; when of such consequence, that their lives, as well as their healths may depend upon it."

The proposals are followed by "Several Reasons for Supporting the foregoing Propositions," [8] which are in fact the propositions in a more extended and detailed form.

In evaluating these proposals it is evident that one very important aspect is the suggestion for the establishment of a systematic connection between the hospital system and the study and practice of medicine. In conjunction with this basic proposal, he also suggests the establishment of special hospitals for specific purposes or for certain categories of disease. It seems likely that Bellers' proposal, to put one hospital under the care of the Queen's physicians so that they would be better able to treat her, was included to gain the support of Queen Anne for his project.

In connection with the proposal to establish a hospital for the blind Bellers suggests that it will improve the quality of the medical personnel engaged in this field of medical activity. He was well aware that the majority of the oculists of his time were ignorant, uneducated empirics. But, he says, "It may breed up some of the best oculists in the world, by their constant attending such a house, having all the additional helps that experimental phylosophy, and a liberal education can give them:

[8] *Ibid.*, pp. 10-17.

which most of our modern oculists want; though several of them have done some extraordinary cures, and are worthy a gratuity from the publick, that their skill may be transmitted down to posterity, in such hospitals as I here propose." [9]

The fifth proposal is one of the most interesting of the entire group, and is an excellent illustration of the far-reaching and advanced character of Bellers' plan. Proposal V is a plea for a national health institute. From the reasons which he advances for the establishment of such an institution it is evident that Bellers was well abreast of the latest developments in medical and biological research. Nor is this very surprising, for John Bellers was a Fellow of the Royal Society, and a friend of Sir Hans Sloane (1660-1753), the eminent physician and president of the Royal Society (1727-41).

In support of his proposal for a national health institute he points out that " Chymistry hath produced many excellent medicines so no doubt, but that there are several more that will be discovered." Furthermore, that " the blood, urine and saliva, in every distemper and age, may be chymically examined in their texture, quality and tincture; and also by microscope, air-pump, hidrostaticks, as well as by every sort of drug, mineral and metal; as spaw-water is tried by Gauls.

" And also, exact observations to be made on the pulse, which Sir John Floyer hath begun a good introduction to; it being of great consequence, for physicians to judge of the state of their patients by." [10]

In conclusion, we may sum up the substance of Bellers' argument and proposals as follows: Illness and untimely death are a waste of good human material. The health of the people is so extremely important to the community that it cannot be left to the uncertainty of individual initiative, which the high incidence of curable disease shows to be inadequate to the task of dealing with this social problem. Consequently, Bellers puts forth proposals for the establishment of hospitals to be used as teaching and research centers, for post-mortem examinations, for the erection of a national health institute, and for the provision of medical care to the sick poor.

Clearly, John Bellers was a man ahead of his time, for even today some of his proposals are still to be realized. The very boldness of his conception compels our admiration. Despite the fact that his proposals apparently had no tangible results, he certainly deserves a permanent place in the history of medicine, particularly as a pioneer in public health.

[9] *Ibid.*, p. 13. It was not until almost two centuries later that the first special eye hospital was established in London thus realizing Bellers' suggestion.

[10] *Ibid.*, p. 14.

THE STRUCTURE OF THE CLINICAL HISTORY

W. RIESE

A FORERUNNER

Disease being a chapter of natural history the physician who takes a clinical history becomes by this very fact a historian. As will be shown in this paper he necessarily adopts methods the historian uses in his effort to analyze and to write a chapter of history. A systematic attempt to interpret the clinical history in the light of its intrinsic *historical* character has been made by O. Temkin.[1] In his important paper he traced the passage from the Hippocratic origin of the clinical history as of the individual history of a human being who suffers and who has symptoms, to that later and secondary product of nosology and classification which is no more the history of a particular case but that of a particular disease or species (historia morbi). He further stressed the still fragmentary character of the Hippocratic clinical history and the historical process of its enrichment in the course of centuries. The sharp demarcation of the patient's subjective statements and the physician's objective status, made under the growing influence of pathology, brought this evolutionary process to an end and became responsible for the actual type of the clinical history. It is to the credit of our author to have recalled to our mind that what is generally believed to be the objective (or "exact") nature of the physician's statement still comprises a very problematic element, precisely the physician's own subjective approach. Temkin also endeavored to analyze the *procedure* the physician adopts in his effort to take a clinical history. I believe that the most valuable and the most fecund element of this attempt is to be seen in his pointing to the physician's effort to make a *selection* among the data the patient may give, to neglect some of them, to insist on others, and to assign to each fact, meaningless when isolated, its place in a whole. It is the primary purpose of my paper to submit this choice as *the first and most fundamental step of the physician's entire action* to a rational analysis; but this will necessarily require a pre-examination of the intellectual procedures involved in this choice. According to O. Temkin, the principle the physician adopts in this selection, is "the idea of the clinical history as a

[1] Studien zum "Sinn"-Begriff in der Medizin. *Kyklos*, *2*: 21-105, 1929.

whole" (p. 62). In describing this whole as being determined by its parts (or organs: "Glieder") and the parts as obtaining their significance ("Sinn") from the whole, our author chose the principle of the organism as the model on which to conceive and to construct a clinical history.

RATIONAL INTERPRETATION OF THE ORGANISM, ESSENCE AND LIMITS OF ITS HISTORICAL NATURE

An attempt will now be made to arrive at a precise idea of the organism and to examine whether this whole is an appropriate model of historical evolution. The usual assumption that a whole cannot be divided, is but a negative statement; that it is more than the parts taken together is an unsatisfactory one, because we just want to know why this holds true. *Empirical data being only rhapsodic or fragmentary, a whole is always the result of our effort to synthetize and to coordinate natural phenomena.* Obviously, this presupposes a coordinating principle. But again, reason and not nature is the birthplace of principles (we cannot include reason in nature, because we cannot make the instrument we use in our attempt to interpret organized nature a part of the subject to be investigated). We have no *immediate* knowledge of the organism as of a product of nature; but we have immediate knowledge of our own intellectual organization, this knowledge even being the only immediate knowledge we have. We thus can only *interpret* the principle of the organism as analogous to that coordinating principle we detect in ourselves.

Coordination is due to an acting *cause*. But the causality here involved is not the category, most precious instrument of human understanding by means of which we fix *the chronological and irreversible sequence of two events*; the causality we use in our attempt to interpret organized nature is a *productive* and not a purely chronological principle. It is an *idea* rather than a category. The latter, however, still remains the *instrument* by means of which the raw material is coordinated. How could a product of nature indeed be organized were the raw material not supposed to be submitted to the goals of the organizing agent and to its quasi intended and anticipated effects? In other words we give to an idea (Ens rationis [2]) an *executive* power and here we are dangerously exposed to dogmatic vitalism, our way of talking becoming easily a way of thinking and a principle of reasoning becoming a concrete entity. Unless we conceive this productive agent as residing outside the organism (thus yielding to

[2] This term was used by Kant in his opus postumum which the reader may consider as the matrix of the doctrine of the organism here outlined.

ontology) we must endow each part of the organism with this agent although we have no knowledge as to the nature of this endowment. Then each part holds the chief position of the productive agent and *this alone makes the part an organ.* It now not only grows by its own, but being endowed with the directing principle, it exerts its influence on the growth and the activity of all the others endowed with the same principle; and it undergoes in its turn their influence. This is what may be called a *self-regulated and self-created whole and no other meaning can be given to the organism unless we yield to metaphysic speculations. The rational principle of this interpretation is the reciprocal and organogenic relationship of the parts.* This relationship may be expressed in terms of *correlation* or *consensus*, provided we give full credit to the *organogenic* nature of this interdependence. Genesis, growth, regulation, coordination, are total behaviors, they necessarily appeal to all of the parts of the organism. This universal cooperation converges towards a final action in which the various components no longer appear *as such*, thus being a *unifying* action. Movement *as such* contains neither muscles, nor nerves, nor glands, although the latter ones cooperate in the final result which, however, can only be described in its own terms. Again we borrow this unity from our own organization and we interpret the organism's unity as analogous to our own acting self; but this self is devoided of any material quality and contents. It is neither chronological nor spatial in character (as Kant has recalled to the physician in his comment of S. Th. Soemmerring's "Organ of the Soul," 1795), it therefore has *no history at all*, the accomplishment of history requiring space and time as the media in which alone history can be made and concrete beings living in those media and undergoing changes. But as far as the raw material to be unified is concerned, vital phenomena and stimulating events, the organism is a historical whole. In limiting the historical nature of the organism to its spatial and chronological manifestations, we open to it but one world, i. e. the world of our experience. But this is the only world we have and it is an inexhaustible one.

HISTORY IMPLIES CAUSALITY

The organism being a whole displaying its manifestations in time and space, indispensable media of historical evolution, and this whole being submitted to a productive (or organogenic) as well as to an instrumental causality, it can be asserted that history does not contradict causality. The clinical history being the first step in a whole of reasonings and actions aimed at treatment and healing, and the search for causes being an indis-

pensable element of a rational treatment, the clinical history cannot but be at the service of the search for the causes of disease. The idea of the clinical history as of an " organismic " whole is but the result of an *interpretation* although a very fortunate one. But it cannot contribute to the *investigation* of the material and concrete causes as of factors and events foreign to the organism. It is justified and necessary to integrate a given disease in the whole of an individual life. But no pathology can ever repudiate the existence and cooperation of pathogenic factors threatening and invading the organism. Indeed, in interpreting disease *exclusively* as the symbolic expression of individual (or collective) tendencies, we adopt the view of a self-destructive life and we give up the historical approach, external events and the internal *changes* they produce being milestones of historical evolution.—In the beginning of this century medical writers made a great and successful effort to study the law of causality as to the special type and use it reveals in biology, a similar attempt having previously been made by A. Schopenhauer on philosophical grounds.[3] These efforts converged towards a movement called " conditionalism " which was almost entirely limited to Germany and which suddenly vanished from the literature, about the time when the profound changes the post-war world had to undergo in every respect and in every field of human action and thought, brought new problems to the stage. It is to the credit of the conditionalism to have recalled to the attention of the contemporaries that in the science of life a given phenomenon is never determined by a single cause but always by a *multiplicity* of causes. The statement that each of those " conditions " is *indispensable* for the final effect is another important element of conditionalism, leading to the conclusion that identity of effects results from identity of the whole of determining factors. Obviously, the conditionalism was wrong in assuming that all of the conditions necessary for the final result, were equivalent (Verworn[4]); here it maintained more than could be proved, no *objective* criteria being available admitting of any determination of the " values " to be attributed to each of the various conditions. Furthermore, those conditionalists were wrong who tried to " replace " the causalism by the conditionalism, conditions being only types of causes, their use presupposing the causal thought for which therefore the thinking in terms of conditions cannot be substituted. Finally, conditionalism failed to realize that in biology each event has a causality *of its own*, admitting of no identity of two causal series, the ele-

[3] Über die vierfache Wurzel des Satzes vom zureichenden Grunde.
[4] *Kausale und Konditionale Weltanschauung*, 1918, Jena, G. Fischer.

ments of which are not interchangeable. But *a great deal of effort could have been spared* by keeping alive the two essential results we owe to conditionalism, namely that in biology there are always multiple causes at work, and that all of them are indispensable for the effect. A conditionalist would not have disagreed with Temkin's statement that a historical whole is in its very nature a "deeply-rooted whole" ("weitverzweigter Zusammenhang": p. 39); the conditionalist would only have submitted that by its deep roots a whole does not exclude but that it implies causality. *Causality is the only means at our disposal by which we array phenomena irreversibly. Causality thus determines the march of time.* Time *as such* is but an empty medium admitting of no discriminative qualities. Only after establishing an irreversible order of *events* the objective evidence of which is witnessed, we give to terms such a "precede" and "succeed" their meaning; but here we necessarily use the law of causality. Thus, there is no historical whole worthy of this name, not submitted to causality.[8]

THE METHOD OF ANALOGIES

History is not a chaotic assemblage of facts but an orderly sequence of events. Indeed there would be no history if its elements were not related to one another so as to form an intelligible whole. Willingly or unwillingly the patient who traces the history of his illness and the physician who takes this clinical history adopt the same method. It is true that *a clinical history should always tend to be a life history, a disease being the final result of all the factors which modelled this life.* Since we can never deny to a clinical history to be the history and the final result of an *individual* life, the Hippocratic type is not only a *historical* but at the same time the *basic* type of the clinical history. The patient will be encouraged to give a narrative on a basis as broad as possible and the life history will

[8] Not satisfied with opposing a "genetic" whole to a "causal" one, Jaspers asserted (in his *Allgemeine Psychopathologie*) that only the former is "conceivable" ("verständlich"), while the latter is unconceivable, though "regular" ("gesetzmässig") and thus "explicable" ("erklärbar"). But genesis implies causality. Thus, "genetic" and "causal" are no antithetic terms. We were told that certain phenomena can only be "explained" (causally) but not "conceived." But as far as the *changes* are concerned to which natural phenomena (organized or not) are constantly submitted (changeable phenomena, being what we call the march of events or history), there is only one approach to conceive them: the causal thought. As soon as I have succeeded in relating one event to another or to a series of others as to the necessary conditions of its appearance, I have conceived it, and nothing is left for me to do. Therefore "conceivable" and "causal" are not antithetic terms.

always overshadow the clinical history. *It is not the history of the disease which leads to an understanding of the life history but the latter which may induce an understanding of the former.* In the combined effort of patient and physician there is that permanent and sometimes only suspended readiness to go back to the life history. This readiness makes one of the most important elements of the art to give and to take a clinical history. But this is only the first step in our effort to obtain a clinical history worthy of its name. The second step will be to restrain the patient from indulging in this attempt. Now, the biography will be studied and written only as far as the illness and its course are involved (Temkin, p. 64). But then we approach the critical situation where a selection must be made and where the problem comes up to know *how to make this selection among the confusing and abundant facts available in everyone's life.*

The choice is made according to what may have contributed to the outbreak and to the development of the disease, its origin, mode of onset, mechanism, course, exacerbation, remission, return, duration, improvement or impairment, dependence upon other factors and presumable outcome. The *causal* nature is obvious in those of the mechanisms quoted above which are proper to etiology and prognostics. It seems less obvious in those terms describing the historical nature of disease, here I must refer to the preceding chapter of this paper. As a matter of fact, in some causal mechanisms, such as in hereditary, predisposing and constitutional factors, causality appears no longer in its purest form but as its derivatives; we are inclined to consider them as "remote" or "non-essential" causes. But there are no *objective* criteria according to which essential causes can be distinguished from non-essential ones.* *The guiding principle according to which the search for causes is made, are the subjective experiences of the patient and the previous objective experiences of the physician.* To begin with the latter ones: While taking the clinical history, the physician is constantly guessing the nature of the disease and searching for its causes, although this constant effort may escape his own attention and control. The whole of his former experience and of his training is present to his mind and from the beginning the actual case is interpreted in the light of this whole. Again, while taking the clinical history, he is wavering between several decisions as to origin, nature, and causes of the disease, giving up one way of explanation, entering another, going back to the former, leaving it open at the next moment and reaching a conclusion which still may be a preliminary one. Here the march

* See W. Riese: Claude Bernard in the Light of Modern Science. *Bull. Hist. of Medicine*; *14*: 281-294, 1943.

of the physician's reasoning unfolds a *genealogy of the methods* the human mind uses in all its efforts to understand and to interpret natural phenomena. At first approach it concentrates on the immediate events as on the presumably exclusive causes of disease and this marks the *dogmatic* method. Then, in trying the contrary, and in considering all conceivable causes supposed to be equivalent, it becomes a *sceptical* method. It finally reaches the stage of *critical* reasoning by trying to make a selection among the preceding events. The method the physician now applies (usually unaware of his being a systematic thinker using the treasure of his entire knowledge and rational faculties) *is the method of analogies,*[7] *the actual, still unknown causal relations indeed being interpreted in the light of former, well known and solidly established ones.*

Not only *historical* science, but also *jurisdiction* as far as concerned with the search for the causes of nervous disorders succeeding accidents have adopted the method of analogies.[8] But the latter is nothing more

[7] The method of analogies has been designated as "a mighty instrument" in historical research by F. Schiller in his academic lecture: "Was heisst und zu welchem Ende studiert man Universal-geschichte," 1789. It is comprised implicitly in Hippocratic medicine. It seems that the acuity of thinking and the philosophical approach so characteristic of the French school, has enabled French physicians more than others to detect the method of analogies in Hippocratic medicine. I quote from the *Dictionnaire Historique de la Médecine Ancienne et Moderne*, by Dezeimeris, Paris, 1836, the following passage devoted to Hippocrates:

"Etudier un à un les faits qui constituent le domaine de la médecine, c'est-à-dire, les cas morbides, les rapprocher selon leurs analogies de cause, de marche, de tendance et de terminaison, exprimer en aphorismes les résultats généraux que l'induction saisit dans ces rapprochemens, telle est la manière de procéder dont on reconnait les traces indubitables dans les *épidémies*."

Hippocratic medicine comprising a vitalistic element, one will not be surprised to read the following sentence in P. J. Barthez's *Nouveaux Eléments de la Science de L'Homme* (Paris, 1806): "Expliquer un phénomène, se réduit toujours à faire voir que les faits qu'il présente se suivent dans un ordre analogue à l'ordre de succession d'autres faits qui sont plus familiers, et qui dès-lors semblent être plus connus" (p. 7-8).

[8] Since the definition of what is called an "adequate cause" is nearly identical in the jurisdictions involved, I will only quote the original text of the Swiss federal jurisdiction:

"En effet, d'après la théorie de la causalité adéquate, à laquelle le tribunal fédéral parait se rallier dans le dernier état de sa jurisprudence, on ne doit regarder comme la cause d'un dommage que les actes qui, d'après les données de l'expérience étaient généralement propres à amener le résultat dommageable et l'on doit dénier la qualité de cause (au sens juridique de ce mot) aux conditions qui ont contribué, il est vrai, à la survenance de l'effet, mais qui, objectivement, dans le cours ordinaire des choses, n'étaient pas de nature à le produire." BGE (= Recueil officiel) 41 II, p. 34. (Quoted from = Riese, W.: Le problème de la causalité dans la nevrose traumatique. Conférence faite à la réunion de la Société suisse de neurologie à Lucerne, le 13 et 14 nov. 1937. *Archiv. suisses de neurologie et psychiatrie*, *41*: 410-422, 1938.

It is obvious that here previous expériences ("données de l'expérience") were adopted as criteria of the causal nature of a given event. This is analogy.

than the method by which *common sense* proceeds in its attempt to give a causal explanation of a given phenomenon in daily life. In interpreting a man's action *in the light of his previous behavior* we gain insight and understanding of his actual behavior. In anticipating his future behavior on the same ground, we use the method of analogies for prognostics. As soon as we are no longer able to understand our own behavior in the light of previous experiences we made with ourselves, we lose the continuity of our historical existence (this may be a premonitory sign of imminent crime or psychosis). It is true that by the method of analogies we gain no *absolute* certainty as to the responsible (causal) agents of a given event. In historical science (science of life being a historical science), phenomena do not reappear a second time identically, therefore they cannot be reproduced at will by an experimenter. The only way of establishing their causality is by reproducing them in the mind of the physician and in the light of *analogous* experiences. But since in life there is only analogy but never identity, this implies a certain unsecurity which cannot be ruled out and which is due, not to the unsecurity of the *law* of causality, but to the deficiency in our knowledge of *conditions*, due also to the fact that in historical sciences each event has a causality *of its own*, thus being always a first and a new event. Nevertheless, *the method of analogies is the only one we dispose of to establish causal relations in life and history.*

We have now to consider the patient's attempt to submit his actual condition to his own causal interpretation. In this attempt he would apply the same method as the physician, i. e. the method of analogies. Let us presume that the disease he experiences is a first and not a recurring one, so that there are no previous experiences in the light of which the actual condition can be interpreted as analogous to the former ones. Then he will go back to previous experiences made by others and to that kind of medical knowledge present to the mind of the average man endowed with common sense and some educational background. But he might make a first experience *of his own*, and why should the patient not make a discovery? There may be agreement between physician and patient as to the choice of the facts and events being the milestones of the clinical history. But frequently the patient will give a causal history of his own, insisting on interior experiences and subjective signs which he cannot but consider as the first enunciation of things to come. It may well be that he is mistaken as to the *causal* importance of those facts. But he will never be mistaken as to the *existence* of them, the patient being the only witness of what happens to him. *The description and the natural history of all he felt and he still feels will therefore be the most valuable*

element in the structure of the clinical history given by a sincere individual. Nobody would deny the eminent role onset, nature, localization, course and rhythm of pain play in a clinical history and in any disease, and still the patient alone is able to make those statements based on his own experiences not shared by anyone else. Disease may be characterized by the appearance of symptoms not existing before, *symptoms indeed being new-formations in the whole of vital manifestations a given individual may reveal. Pain and discomfort generally being the first symptoms (although only subjective ones), their chronological and qualitative analysis is the first and the decisive step in our attempt to delimit the constituent elements of a clinical history from the innumerable but less important facts and events constituting a life history.* Again, to give full credit to subjective signs is not only an element proper to the *hippocratic* as to a *historical* type of clinical history; it is at the same time a *basic* principle of the structure of the clinical history as such. *Medical action starts with subjective facts and no objective statement can be made, no diagnosis and no therapeutical plan, unless those subjective facts are given their full consideration and significance.*

EPILOGUE

The unfolding of the patient's life and of the conditions responsible for his actual state cannot but have a reciprocal influence on this state and thus become a *therapeutic* agent. Here is the point where the two different and apparently opposite branches of medical art join each other. This medical art indeed is indivisible in itself and only by habit and mode one of its elements may come to the foreground, others be neglected. Thus, it seems as though modern times have created the research physician, isolating him from the treating physician. It is true that social conditions and the ever increasing experimental procedures may not allow the same physician to be both at the same time; but this is only a technical hindrance. As a matter of fact, *the physician who makes an inquiry about sources, background and immediate causes of a given disease, does research work and applies necessarily the principles of the experimental method* (*Claude Bernard*). The essence of this method being the determinism of vital phenomena, one will not be surprised to see the inquiring physician becoming a treating physician since his inquiry is necessarily a *determining* factor and may thus induce a change in the patient. *The art of taking a clinical history thus becomes the art of treating a patient.* But a clinical history comprises also a basic element of *pathogenetic* factors

common to all times, such as birth, trauma, evolutionary disorders and crisis, nutritional deficiencies and dietary digressions, emotions, infections, intoxications, etc. Due to these very general factors clinical histories can be read and used at all periods of history. Indeed, diagnostic and therapeutics undergo permanent variations, they are submitted to the influence of modes and they drive to despair those who want to assign to medicine a scientific character. It seems to me that the clinical history, its structure and the basic element of pathogenesis it comprises, are still among the best witnesses of medicine as a *science*.

ADDENDA

The historical view of diseases being an intrinsic feature of Hippocratic medicine and the *age* of the patient being an outstanding fact supporting such a view, one will expect *Hippocratic pathology being written in terms of life periods*. I do not know whether full credit has already been given to this aspect of Hippocratic medicine. But I do know that no systematic attempt has been made so far to write a clinical pathology in terms of life periods, although such an approach would yield new aspects and discoveries and new ways of treatment. In Hippocratic medicine the various life periods, their behavior, constitution and reaction types are interpreted in the light of their proper physiological processes (*Aphor.* I, 14). Each of those life periods requires a diet of its own (*Aphor.* I, 13, 16, 17). The various life periods have an affinity of their own to the various places and seasons (the latter ones being indeed the great historical periods of the year). In a given district and in a given season persons of a given age are more liable to certain diseases than persons of another age (*Aphor.* III, 3, 18 and *Airs, Waters and Places*). Longevity too is in function of place and season as well as premature ageing. The predilection certain diseases show for certain life periods is stressed with emphasis (*Aphor.* III, 24, 25, 26, 27, 28, 29, 30, 31, VI, 57). Each disease may have a symptomatology and an outcome of its own according to the life period in which it may occur (*Aphor.* I, 14, II, 39, 40, VII, 82) and the chance of treatment is in function of the life period in which a given disease appears (*Aphor.* II, 45).

In Hippocratic medicine a clear distinction is made between constitutions and disease, the former ones being structural types and behavior patterns, which, in their turn, may be " subject to " certain diseases. But disease is always a *new* event, in spite of the affinity certain constitutions show to certain diseases. Disease is due to the action of factors foreign

to the organism. In his constitutional physiology and pathology, the great Greek did not abandon his historical approach. Constitutions are traced back to their causes and considered to be in function of place, seasons, nature of the soil, usage and even political institutions, warlike and courageous behavior, proper to independent and self-determining nations, being submitted to change in a despotic institution (*Airs, Waters and Places*). Generally speaking, constitutions are thought to be flexible. If a given custom (such as fashioning the head of the new-born child) no longer prevails, the long head disappears. The fatalistic and antihistorical idea of constitution as a necessarily inherited and unchangeable character, so characteristic of many modern writers and naturalists, is foreign to Hippocratic medicine. According to the latter, constitutions are acquired, and such an acquired disposition may indeed be transmitted to the descendants but also disappear if the causes responsible for their appearance are no longer active.

Man's history studied in the light of modern natural science, does not start with man himself but with the ancestors of his race and his species. And so does the clinical history. Symptoms are traced back to prehistorical ages, the abandon of ancient habits and the repression of primitive or archaic tendencies being held responsible for actual discomfort, suffering and disease. J. J. Rousseau was the first pioneer of the doctrine according to which man approached the decline of his former strength and health at the very moment he gave up his life as a "savage". and abandoned his natural customs and mode of life in order to build up culture, sciences, and art. No place is left in this picture to the physician, the great French philosopher being definitely hostile to medicine and doctors. In the nineteenth century F. Nietzsche had a similar view of mankind, being on the road of its decadence because it frightened from its original brutality, violence and aggressiveness, all of which were considered as signs of force and health. Although S. Freud was always anxious to eliminate values from his doctrine, he also saw mankind struggling with its prehistorical heritage and losing its psychical health by its constant and vain effort to overcome the primitive still alive in it. *The common element in all these doctrines and their numerous derivatives is the idea that man has become ill by sacrificing the habits of his hypothetical ancestors, the latter ones linking him with the whole of living beings and with what is understood to be "pure" nature. But it seems to me that Hippocratic medicine differs fundamentally from those doctrines.*

In Hippocratic medicine this problem is discussed as a problem of diet. But the search for food being one of the primitive and imperious tendencies to which a living being is submitted (the striving for sexual objects being another one), it makes no fundamental difference which of those two tendencies may be considered as favorable to health when satisfied in its presumably original manner or as dangerous to welfare and well-being when abandoned in favor of new and culture making habits. In Hippocratic medicine the view is adopted that man, as long as he might have used "strong and brutish diet, swallowing things which were raw, unmixed and possessing great strength," must have suffered much and severely and become exposed to strong pains and diseases, and to early deaths. Thus, the search for a food "befitting their nature" became a necessity, but they succeeded only after a long lapse of time. Medicine was invented when man discovered the food proper to the sick. The very astonishing and enlightening statement is added that the primitive mankind would suffer less from primitive food than we would now (but still it would suffer severely). In other words, *there is no way back to ancient habits, unless the actual mankind takes the risk of new and severe sufferings*. This is what may be called the answer of the Greek to any encouragement to abandon cultural habits and to guess primitive satisfactions. Generally speaking, *if man suffers from culture, he will not be better off by deserting culture*. Man becomes sick when sticking or returning to his old habits, and the new habits he discovered after a long period of effort and trial, are guarantees of health, welfare and culture.

Thus, mankind itself is the measure of its needs, satisfactions and realizations, and if mankind in its true nature starts with culture, the principle adopted in Hippocratic medicine may be called a *humanistic one*.[9]

[9] Ratio being an intrinsic element of human nature the humanistic principle comprises the rational one as its corollary. The all-importance of systematic *reasoning* is stressed in the following quotation: ". . . I say, we ought not to reject the ancient Art, as if it were not, and had not been properly founded because it did not attain accuracy in all things, but rather, since it is capable of reaching to the greatest exactitude by reasoning, to receive it and admire its discoveries, made from a state of great ignorance, and as having been well and properly made, and not from chance" (On Ancient Medicine). The law of *causality* being the most important instrument human understanding has and uses in its effort to submit natural phenomena to analysis and explanation, *Hippocratic medicine is necessarily causal in its very nature*. It goes without saying that the etiological element in Hippocratic medicine presupposes causality. However, in Hippocratic medicine prognosis is given a leading role. But prognosis means anticipation of things to come by studying the actual situation which thus is thought to be the *causal* agent of the future. Furthermore, the Hippocratic definition of nature as of a "restoring principle" implies a causal element, since restoration is due to an acting cause. Galen

Although Hippocrates had laid down the principles of a historical study of diseases, the explicit task of making suggestions how to proceed in asking the patient, was left to a forerunner of Galen, Rufus of Ephesus.[10] His treatise " On the Interrogation of the Patient," is small in extension but unusually rich in content. It is significant that the first outlines of a technique of interrogation contain already an analysis of *pain*. Obviously, the author wants to draw the attention of the reader to pain as to a phenomenon of major importance, the full significance and nature of which can only be established by interrogation. However, the objective manifestations of pain and their enlightening character are not neglected and an attempt is even made to distinguish pain from simulation. Further suggestions " *How to detect malingerers* " will be given by Galen.

Generally speaking, the emphasis laid by the Greeks on reliable criteria of truth, shows how much *they were inclined to assign to the patient's own statements their full importance and how anxious they were to use those statements as basic elements in their diagnosis and constructive reasoning.* Therefore, to them simulation was a *problem* to be solved and not only a moral defect to be punished by the physician.

kept this tradition alive as shown by his polemic remarks against the a-causal treatment of the methodists (*On the Medical Sects*: For Beginners, Chapters VII and VIII) and some significant passages in his *Natural Faculties* (p. 197 and p. 199). Finally, I quote Sydenham: " But our misfortune proceeds from our having long since forsook our skilful guide *Hippocrates*, and the ancient method of cure founded upon the knowledge of conjunct causes, that plainly appear: insomuch that the art which is at this day practised, being invented by superficial reasoners, is rather the art of *talking* than of healing " (*The Entire Works*, XX, London, 1769).

[10] *Greek Medicine.* Being extracts illustrative of medical writers from Hippocrates to Galen, Translated and Annotated by Arthur J. Brock, London and Toronto, J. M. Dent and Sons, Ltd., New York: E. P. Dutton and Co., Inc., p. 112-124.

THE HISTORY OF ELECTRODIAGNOSIS

SIDNEY LICHT

The characteristic response of living tissues to electrical stimuli in health, and the patterns of variation in disease have led to a system of investigation called electrodiagnosis. Physicians have played an important role not only in the diagnostic development but in the discovery and progress of electricity itself.

William Gilbert of Colchester was a practitioner of medicine whose ability won for him the distinction of physician-in-ordinary to Queen Elizabeth, together with the leisure and honorarium which he spent most profitably in research. His investigations in physical science were concerned with natural and frictional magnets, which had become a popular study among the philosophers of the sixteenth century as a result of widened navigational horizons and the concomitant interest in the compass. His findings and conclusions incorporated in *De Magnete*, published in 1600, mentions for the first time the "electric force."[1] His coverage of the subject was so exhaustive and careful, that nothing original was added to his observations for decades. The concept of tissue response to stimulation had not yet made its appearance, and neither Gilbert nor his contemporaries thought of applying the newly named energy in this manner.

In 1658, Jan Swammerdam amused his patron of science, the Duke of Tuscany, with the twitches of an isolated frog muscle, by pinching and cutting its nerve.[2] He described this performance as a "most delightful

[1] Gilbert, William—*De Magnete*. London 1600—Translated by P. F. Mottelay. New York, 1893, p. 85. Gilbert's work was remarkable not only for its frequent examples of inductive philosophy which preceded the publication of Bacon's *Novum Organum*, but for its emphasis on the experimental approach to science. "Men of acute intelligence, without actual knowledge of facts, and in the absence of experiment, easily slip and err." *Op. cit.*, p. 82.

[2] Nerves have since been stimulated as well by tapping, temperature variations, chemical applications, electricity and compressed air currents.—Allen, F. and Hollenberg, A.—*Quart. J. Exp. Phys.* 1924, v. 14. p. 351. Clinically, electricity has been found most satisfactory because it meets the conditions of a stimulus which "should be capable of uniform repetition, of increase or decrease by definite amounts . . . and of such a nature as to cause no injury by which the excitability of the tissue might be changed in some unknown degree."—Bose, J. C. *Comparative Electrophysiology*. 1907.

and indeed equally useful experiment." [3] In the light of later developments, some authors had considered those muscle contractions as the response to electrical stimuli because metal instruments had been employed, but an examination of Swammerdam's illustrations,[4] fails to reveal the possibility of a closed circuit. In 1700, Duverney, a French anatomist, performed for the first time what is now perhaps the most universally performed experiment of the physiology class-room; the electrical stimulation of frog muscle.[5]

Towards the middle of the eighteenth century, the results of several investigators were published on their studies of tissue stimulation.[6] Pacchioni [7] noted how a trephined dog " twisted itself in all directions " when he stimulated its brain directly with cotton dipped in different irritating solutions. Interest in the subject of experimental muscle physiology was universally aroused by the publications of Haller's numerous observations which established the fundamental principles of peripheral nerve function.[8]

The first report of purposeful muscle contraction with static electricity is attributed to Kratzenstein of Halle in 1745.[9] In 1747, Jallabert [10] produced muscular contractions for the purpose of exercising them and found that the muscles of a paralyzed arm, although deprived of sensation and motion for some time, could " be made to move at my will in a very pronounced manner." During this period anyone who owned an electric generator felt qualified to practise electrotherapy, and the Abbe Nollet was " curing " paralytics with static electricity. When Louis, chief surgeon at the Salpêtrière was unable to repeat these results, Nollet the

[3] Swammerdam, Jan—*Biblia Naturae.* Leyden, 1738, v. 2, p. 839.

[4] *Ibid.*, Table XLIX, Fg. V.

[5] Duverney, J. G.—*Histoire de l'Acad. des Sciences.* 1742, v. 1, p. 187, in Mottelay, P. F.—*Bibliographical History of Electricity.* London, 1922, p. 148.

[6] Francis Glisson (1667) contracted the muscles of recently killed animals by stimulating them with corrosive fluids and cold. He was the first to mention irritability as a property of tissue.—*Tractatus de ventriculo et intestinis.* Lugduni Batavorum, 1691, p. 168. Whereas Glisson included even the blood among irritable tissues, Haller limited it to the " capability of muscle to contract when stimulated as the result of vital force." John Brown called the capability of tissue response to stimuli, excitability.—*The Elements of Medicine.* London, 1803.—In Verworn, M.—*Irritability.* New Haven, 1913, pp. 2-7.

[7] Pacchioni, Antonio—*Opera.* Romae, 1741, p. 10. Unpublished translation of Dr. Saul Jarcho of New York City.

[8] Haller, Albrecht—*Mémoires sur la Nature Sensible et Irritable.* Lausanne 1756, v. 1, p. 222. " Experiment 179. I cut the nerves of the thigh posteriorly. The thighs lost their sensations entirely, as well as their voluntary movement, but the muscles they supplied remained irritable."

[9] Colwell, H.—*An Essay on the History of Electrotherapy.* London. 1922, p. 19.

[10] *Ibid.*, p. 20.

cleric was piqued into the inadequate response, "Is electricity your field?" [11]

A few years later Whytt wrote that "the power of (electric) stimuli in exciting the muscles of living animals into contraction is greater than any effort of will" and "what will prove a stronger stimulus to the nerves of one part will more weakly effect those of another and vice versa." [12] In 1758, Beccaria [13] noted that the contractions arising from electrical stimulation were stronger than those observed from mechanical stimuli.

In 1784, Cotugno recorded the story of a student who insisted that he had received a strong electrical shock when the scalpel with which he was dissecting a mouse, touched one of its nerves.[14] The subject of animal electricity was in the air. Thus in 1786, when Galvani's attention was directed toward the twitching extremities of a freshly killed frog, he hastened to imagine that all animals were endowed with a native electricity which he could render active by arming their nerves and muscles with metal plates.[15] He ignored the static electricity generator which was present in the room, as well as the fact that the skinned frog was resting on a metal plate. He performed many experiments on the reactions of frog muscle to metals which he described in his classic protocols in 1791.[16] This treatise on communicated and natural animal electricity fired the scientific minds of Europe with the announced discovery of a general law of nature which regarded the brain as the fountain-head and the muscles as reservoirs of electric fluid, conducted thence by the nerves. Everybody who was anybody in science rushed to repeat the experiments,[17] and the immediate reactions among most was one of confirmatory admiration.

Among those who disagreed with this concept was Valli [18] who ques-

[11] Nollet, J. A.—*Recherches sur les Causes Particulières des Phénomènes Électriques.* Paris, 1749, p. 33.

[12] Hoff, H.—Galvani and Pre-Galvanian Electrophysiologists. *Ann. Science*, 1936, v. 1, p. 162 and Fulton, J.—*Muscular Contraction.* Baltimore, 1926, p. 32.

[13] Colwell, *op. cit.*, p. 30.

[14] Wilkinson, C. H.—*Elements of Galvanism.* London, 1804, p. 3.

[15] *Ibid.*, p. 7.

[16] Fulton, J. F. and Cushing, H.—A Bibliographical Study of the Galvani and Aldini Writings on Animal Electricity. *Ann. Science*, 1936, v. 1, p. 239.

[17] Matteucci, C.—*Lectures on the Physical Phenomena of Living Beings.* Translated by J. Pereira. Philadelphia, 1848.

[18] Valli, E.—*Experiments in Animal Electricity.* London, 1793, p. xii. "In the explanation of the mechanism of the muscular motions which arise from the action of the mind, I have by no means followed the theory of M. Galvani." Valli later agreed with Galvani but Pfaff, Van-Marumm and Ackerman agreed with Volta. Cassius, *op. cit.*, p. 6.

tioned Galvani's identification of nervous fluid with electricity. Alessandro Volta, professor of Physics at Pavia, was sufficiently impressed when he first read Galvani's work to write (1792) that "it contains one of the most beautiful and surprising discoveries, and the germ of many others." [19] But by the following year he summarized his objections with, "It is thus that I have discovered a new law, which is not so much a law of animal electricity (most of the phenomena would appear from the work of Galvani to belong to forms of spontaneous animal electricity) but they are in reality the effects of a very weak artificial electricity which is excited in a manner of which there is no doubt, by the simple application of two plates of different metals as I have already indicated." [20]

Monro (secundus), the famous Edinburgh anatomist agreed [21] with Volta that metals had to be connected to each other and to the muscle in a complete "circle," and Fowler [22] confirmed that "convulsions are not excited unless the metals are in contact with each other, and unless both metals are also in contact with the animal substances or the water making part of the circle."

In 1795, Humboldt blistered his own shoulder and applied electricity to the denuded area to prove on his own muscles that their contraction resulted from direct stimulation. He also indicated that the nerve must be intact to achieve such a response.[23]

In 1799, Volta [24] constructed a dependable source of continuous electric current. In his search for a muscle which he could both stimulate and observe closely, Volta showed even greater ingenuity although less courage than Humboldt.

[19] Volta, A.—*Collesione dell'Opera del Cavaliere Conte Alessandro Volta.* Firenze, 1816, v. 2, pt. 1, p. 121.

[20] Volta, A.—An Account of Some Discoveries Made by M. Galvani. *Phil. Trans.*, 1793, v. 83, p. 10.

[21] Monro, A.—*Experiments on the Nervous System.* Edinburgh, 1793, p. 37.

[22] Fowler. R.—*Experiments and Observations Relative to the Influence Lately Discovered by M. Galvani.* Edinburgh, 1793, p. 4.

[23] Cassius, L., Daubancourt et de Saintôt.—*Précis Succint des Principaux Phénomènes du Galvanisme.* Paris, 1803, p. 7. Humboldt first suggested calling the direct current Galvanism.

[24] Volta, A.—On the Electricity Excited by the Mere Contact of Conducting Substances. *Phil. Trans.*, 1800, v. 90, p. 403. "The apparatus consists of 30, 40, 60 or more pieces of copper or preferably silver, each adjacent to a piece of tin or preferably zinc, and an equal number of layers of water or some liquid which conducts better than water, such as saline or soda solution, or pieces of cardboard or leather well imbibed with these fluids, between each pair of two different alternate metals, always in the same order; (voila!) there you have my new instrument which imitates as I have said, the effect of Leyden jars or electric batteries."

47. Happily it occurred to me that we have in the tongue a bare muscle lacking at any rate the thick integuments which cover the other parts of the body surface, a muscle which is not only very mobile, but can be moved voluntarily. Thus I met all the conditions needed to excite life-like movements by the ordinary artifice of the different electrodes (armures). I performed the following experiment on my own tongue.

48. Experiment Q. Having placed some thin strips of tin, called silver-paper, on the tip and upper surface of my extended tongue, I applied the convex part of a silver spoon to the under part of my tongue and inclined the spoon until the base of its bowl just touched the tin-foil. I performed this experiment in front of a mirror and waited to see the tongue quiver. But the reaction which I dared predict did not appear, and in its stead I experienced a strong acid taste at the tip of my tongue.[25]

Volta realized that even though he had not excited motor function he did excite a sensory organ. With the help of the battery which he invented, he was able to overcome the chief cause of his failure which was the sub-threshold current intensity produced.[26] He continued his experiments with stronger currents and noted that "a contraction takes place only at the first flow of electricity, and sometimes also at the breaking of the circuit." [27] In his search for a stimulation threshold he concluded that the muscle response was a more delicate instrument for measuring minute quantities of electricity than the electrometer which was deflected only .001 degrees by an equivalent charge.[28]

Ritter [29] applied electricity to a muscle using a tapped series battery of one hundred cells. He increased the current very gradually by inserting

[25] Volta, A.—Collezione dell'Opere., *op. cit.*, v. 2, pt. 1, p. 158.

[26] De la Rive in his *Treatise on Electricity* (1851) quoted by Duchenne, *op. cit.*, pp. 48-62, has traced the early development of the direct current cell. The columnar pile of Volta was soon abandoned because of the rapid dessication of the circles of cloth which separated the metal discs. This was succeeded by the bulky wooden trough battery of Cruikshank used by Gay-Lussac, and the "crown of cups" used by Davy and Faraday. Berzelius offered a cell in which the copper surrounded the zinc and served as a reservoir for the electrolyte. Daniell (1836) used a porous diaphragm to separate two different electrolyte solutions. Grove replaced the copper of the Daniell cell with platinum and Bunsen substituted carbon for platinum. Siemens used a paste of sawdust and paper between the two solutions. Stöhrer used a cylinder of carbon surrounded by a cylinder of zinc which required but one more step to the LéClanché cell (1868) which is the prototype of the present dry cell.—Benjamin, P.—*The Voltaic Cell.* New York, 1893, p. 229.

[27] Mariannini, S.—Mémoires sur la secousse qu'éprouvent les animaux, etc. *Ann. de chimie et de phys.*, Paris, 1829, v. 40, p. 225.

[28] Cassius, Daubancourt et de Saintôt., *op. cit.*

[29] Lapicque, L.—La chronaxie et ses applications physiologiques. *Physiologie Générale du Système Nerveux.* Paris, 1938, v. 5, p. 23.

one cell after another until full strength was reached, then reduced it slowly through a water resistance, and concluded that if the exciting stimulus was not applied with briskness, the muscle would not contract.

Experiments in electro-physiology were continued by Volta's favorite pupil, Stefano Mariannini, professor of Physics at Venice. In 1829 he found that the ascending (negative) current caused a greater contraction than the descending, which was also more painful.[80]. He spoke of two kinds of muscle contractions; the idiopathic or direct muscle stimulation, and the sympathetic resulting from stimulation of its nerve. He was the first to state that, " When the electric fluid penetrates the nerve in a direction contrary to its ramifications, a sensation is produced." [81]

Pfaff had pointed out certain regular differences in the action of the ascending and descending currents. Ritter developed this concept by distinguishing six stages of excitability based on the degree of contraction following make and break with these currents.[82] Nobili of Reggio, inventor of the galvanometer [83] recognized only four stages of excitation easily identified with those later re-discovered by Heidenhain [84] and subsequently used clinically by Erb.

Carlo Matteucci of Pisa, demonstrated that proximal stimulation of the ligated or sectioned nerve did not elicit a muscle contraction.[85] Matteucci was the last of the great Italian physiologists. His pupil Emil Du Bois-Reymond returned to Germany where, following an exhaustive study inspired by his teacher he wrote the classic *Observations on Animal Electricity*.[86]

Although it was probably a guess on his part, Galen [87] divided all nerves into sensory and motor. In 1810 Bell restated the thought that spinal roots were different in function; that the anterior roots were " insensible " and the posterior roots were " sensible." [88] The final distinction between motor and sensory nerves was made by Magendie in 1822.[89]

[80] Mariannini, *loc. cit.*

[81] *Ibid.*

[82] Biederman, W.—*Electrophysiology*. London, 1898, v. 2, p. 135.

[83] Humphreys, A.—Development of the Conception and Measurement of Electric Current. *Ann. Science*, 1937, v. 2, p. 164.

[84] Heidenhain—*Arch. für physiol. Heilkunde*, 1857, p. 442, in Biederman, *op. cit.*, p. 136.

[85] Bird, G.—*Lectures on Electricity*. Philadelphia, 1854, p. 24.

[86] Du Bois-Reymond, E.—*Untersuchungen über thierische Electricität*. Berlin, 1848.

[87] Galen—*Epitome Galeni Pergameni Operum*. Basle, 1571, p. 184, l. 34.

[88] Correspondence in *Lancet*, 1911, v. 1, p. 697.

[89] *Ibid.*, p. 764.

Magendie's protege, Sarlandiere, proposed the heroic therapy of electropuncture in 1825.[40] A military surgeon of long standing, he had no hesitation in plunging large insulated needles into diseased muscles, and then passing an electric current through them. Under the influence and approval of Magendie, this procedure became a fad throughout France.[41] As with so many other electro-therapeutic modalities since the first announcements of Nollet, ridiculous claims were made for it. As late as 1853, Abeille [42] claimed that after " the respiratory movements of a chloroformed dog had completely ceased, the breathless animal was recalled to life with electropuncture." Magendie tried to introduce the needle directly into nerves,[43] and this was so painful that the treatment lost its popularity. Even before its use was discontinued, critical observers like Hamilton [44] announced that the procedure was used to no avail in many patients with rheumatic and facial palsy. He employed batteries of fifty cells and noted that the magnitude of contraction depended upon the number of cells used.[45]

In 1833, Duchenne became so interested in the procedure of electropuncture that he devoted much of the remainder of his life to the study of electrical stimulation. He soon found that he could stimulate muscles electrically without piercing the skin, and devised cloth-covered electrodes for percutaneous stimulation, the basic design of which is still used. Duchenne called his method of application " localised electrization," [46] and was one of the first to use the alternating current for treatment. He suggested the word " Faradic " to describe that current.[47]

[40] Morgan, J.—Application of Electricity Directly to Nerves and Muscles by Acupuncture. *Lancet*, 1879, v. 2, p. 454.

[41] Duchenne, G. B.—*Treatise on Localised Electrisation.* London, 1871, p. 114.

[42] Abeille, M.—Des accidents produits par le chloroforme et de l'électropuncture comme moyen d'y remédier. *Gaz. des Hôp.*, Paris, 1853, v. 26, p. 619.

[43] Duchenne, *op. cit.*, p. 117.

[44] Hamilton, J.—Trial of Acupuncture With Galvanism. *Dublin J. Med. Sci.*, 1835, v. 6, p. 78.

[45] Most observers of the nineteenth century agreed that an increase in electrical stimulation to a muscle excited increased contraction because the impulses transmitted by the nerves were increased. Gotch suggested that the apparent increase in activity resulted not from a greater contraction of each fiber at each increase in stimulus, but the contraction of more fibers in the muscle.—Gotch, F.—The Submaximal Electrical Response of Nerve to a Single Stimulus. *J. Physiology*, 1902, v. 28, p. 395.

[46] Duchenne, *op. cit.*

[47] Although the discovery of some natural phenomena were unrelated to the studies of previous or contemporary investigators, a careful search of the writings of the period will frequently show that new discoveries are the culminations of the contributions of many. This is certainly true of Faraday's work on induced electricity. In 1819 Oersted

Although Duchenne knew that "there are certain spots along the surface of the body and limbs that give peculiar responses to the electrode in producing ample muscle contraction," he offered no written explanation of what he was accomplishing. In the early phases of his work while he was attempting to establish a routine of treatment, he produced contractions with large electrodes using current of such intensity, that in one instance at least, he admits having produced a fracture of the cervical vertebrae.[48]

Remak [49] explained those "spots or border points" where the muscles were most easily stimulated. The priority controversy between these two men was one of the bitter academic battles of the century. In October of 1852, Duchenne invited Richter, Jacksch, Hebra and Remak to Paris to witness a seance of localised electrization. Although he was able to throw two different muscle groups into contraction at will, he did not explain the technique or rationale to his visitors. When Remak returned to Berlin, he said to its medical society, "One could almost complain of his (Duchenne's) intention to preserve his secret." To this Duchenne replied, "When I experiment in the presence of pupils, I habitually remember to explain anatomical reasons that induce me to place the electrode on this or that point of election, but before the select audience of which Remak formed part, I should have thought it out of place to deliver a lesson in anatomy. Remak saw me produce contractions of a large number of muscles. This great critic obtained no glimpse of the particular methods that allowed me to obtain them. With whom then is the blame?

of Copenhagen discovered "that a metallic wire which communicates with the two extremities of a voltaic cell, acquires the remarkable property of acting at a distance on a magnetic needle"—Hatchett.—On the Electro-Magnetic Experiments of M. Oersted. *Phil. Mag.*, 1821, v. 57, p. 40. In 1822 Ampère announced the conception of current flow.—*Recueil d'Observations Electrodynamiques.* Paris, 1822, p. 15. Arrago magnetized iron by bringing it under the influence of a wire through which a current was flowing, and in 1831 Henry described the augmenting action of a long coil of wire on the direct current.—Colwell, *op. cit.*, p. 56. In the same year Faraday induced current flow in a coil of wire wound on the same iron ring as another coil of periodically charged wire. To prolong the duration of the induced current, Pixii (1832) constructed a rotary magneto-electric generator to which Saxton and others added improvements. Golding Bird credits himself with the invention of the automatic primary circuit breaker (*op. cit.*, p. 115), but Meyer insisted that Neef first added this important element to the induction coil. Rumkorff (1851) designed the inductorium now widely used.—Duchenne, *op. cit.*, p. 296.

[48] Duchenne, *op. cit.*, p. 86.

[49] Remak, R.—*Galvanotherapie.* Berlin, 1858, p. 172. Remak first called attention to the worm-like contraction in denervated muscles.—Zimmern, A. et Pérol, P.—*Electrodiagnostic de Guerre.* Paris, 1917, p. 48.

Did I trust too much to his anatomical knowledge? Remak who has thus represented me as a prestidigitator, says again, ' He owes his knowledge of the points perhaps to chance or rather to trials, by which he arrived at his method! ' Then Remak for the honor of science sets himself to work, and discovers these famous points of election are the points of entry of the muscular nerves." [50]

While this argument was raging, von Ziemmsen in 1857 carefully mapped out the whole surface of the body, marking the motor points on the skin with silver nitrate in agonal patients, and proved by dissection immediately after death, that his clinical markings corresponded with the entrance of nerves into muscles.[51] He published anatomical charts showing all the motor points and lines in a most complete and instructive manner, indicating not only where to apply the stimulating electrode, but the facial expressions which result from the stimulation of individual face muscles. Duchenne's unworthy recognition of this masterpiece was, " We must not praise this work too much, for the writer has fallen under the influence of Remak." [52]

Duchenne may not have discovered why certain points respond to electricity better than others, but he did introduce muscle stimulation through the intact skin, as well as the first electrodes for that purpose. He devised a foot-switch to make and break the current, leaving the hands free to operate the apparatus. He also contributed the knowledge that faradic excitability is diminished in primary myopathies (the Duchenne reaction).[53]

Chauveau, the great veterinarian, confirmed the thoughts of his many predecessors (Bellingeri, Lehot, Phillippe, Michaelis as well as those already mentioned) that the negative is more exciting than the positive pole.[54] He introduced the monopolar method of stimulation in physiology at almost the same time that Brenner introduced it into clinical practice.[55]

[50] Duchenne, *op. cit.*, p. 86.

[51] von Ziemmsen, H.—*Die Electricität in der Medizin.* Berlin 1866. In Colwell, *op. cit.*, p. 97. Doyère (1840) was the first to study histologically the entrance of nerves into muscles. Kuhne showed that all striated muscles possess distinct and similar nerve endings which he called "end-plates." Krause (1868) was the first to suggest that the impulse of stimulation had to pass through the plates to the muscles to produce contraction.—Biederman, *op. cit.*, p. 338.

[52] Duchenne, *op. cit.*, p. 88.

[53] Guillemot, W.—*Electricity in Medicine.* New York, 1906, p. 320.

[54] Chauveau, M. A.—Théorie des effets physiologiques produits per l'électricité transmise, dans l'organisme animale, à l'état de courant instantané et à l'état de courant continue. *Journ. de physiologie*, 1859, v. 2, p. 490, and 1860, v. 3, p. 274.

[55] Brenner, R.—*Untersuchungen und Beobachtungen auf dem Gebiete der Elektrotherapie.* Leipsig, 1868, v. 2, p. 28.

Before the turn of the eighteenth century Galvani had hinted at the possibilities of electrodiagnosis when he stimulated an arm and foot soon after their operative removal. He noted that the foot muscles contracted more forcefully than those of the hand which had been diseased for a longer time.[56] Marshall Hall was the first to direct attention to the value of the galvanic current in the diagnosis of muscle paralysis.[57] Heidenhain had noted that occasionally in the presence of disease a muscle might respond to continuous even though it did not respond to the faradic current. Baierlacher [58] reported that the paralyzed muscles of a patient with facial palsy responded to galvanic but not to faradic current. Schulz [59] and others confirmed this observation, but it was the obscure E. Neumann of Konigsberg in 1864 [60] who offered an explanation. "This result can be explained neither as the result of the quick succession of induced impulses nor the changing direction of the current; the only cause to which lack of muscle response can be attributed therefore is the brief duration of the current."

Wilhelm Erb agreed with Neumann [61] and called the abnormal pairing of nerve reactions to both currents in nerve interruption, the reaction of degeneration (Entartungsreaktion). In 1882 he suggested a further qualification. "Clinical observation has taught that R. D. (reaction of degeneration) is not always completely developed, but that there are cases in which it is incomplete, with the nerve spared to a greater or lesser degree, to which I have given the name of partial R. D." [62] Wernicke later correctly attributed this phenomenon not to partial degeneration of the nerve but to the degeneration of part of the nerve fibers. Erb also studied muscle response quantitatively. He demonstrated that approximately the same amount of electrical energy was needed to contract sym-

[56] Aldini, J.—*Sur l'Origine et les Progrès de la Théorie de l'Électricité Animale.* Paris, 1803, p. 18.

[57] Hall, M.—On the Condition of Muscular Irritability in Paralytic Muscles. *Med. Chir. Trans.*, Series 2, v. 4, in Meyer M.—*Electricity in Its Relation to Practical Medicine.* New York, 1872, p. 191.

[58] Baierlacher, E.—*Bayreuth Aerzt. Intelligensblatt*, 1859, no. 4 in Neumann, *op. cit.*

[59] Schulz, B.—Ueber das Verhalten der Muskeln bei Paralysis Nervi facialis gegen den inducirten und konstanten elektrischen Strom. *Wien. Med. Wochensch.*, 1860, no. 27, p. 417.

[60] Neumann, E.—Ueber das verschiedene Verhalten gelähmter Muskeln gegen den constanten und inducirten Strom und die Erklärung desselben. *Deutsche Klinik*, 1864, v. 16, p. 65.

[61] Erb, W.—Historisches von der Entartungsreaction. *Berl. Klin. Woch.*, 1885, v. 22, p. 765.

[62] Erb, W.—*Handbook of Electrotherapy*, New York, 1883, p. 82.

metrical muscles. During the progress of these studies, he found instances of increased and decreased muscle irritability as evidenced by the quantity of electrical energy required to excite contraction.[63] He found increased irritability in early spinal and peripheral nerve lesions, "but of great interest and importance is the marked increase of electrical excitability in proven forms of spasm; I was the first to demonstrate this in a case of tetany." [64] Mann [65] later showed the critical value to be five milliamperes with the anodal opening stimulus. In his book on Thomsen's Disease,[66] Erb listed its electrical characteristics. Erb is best remembered for the significance he attached to aberrations in the contraction formula.[67] Biederman later explained the inversion of the formula in disease by pointing out that a virtual cathode forms in the region of the anode, and that electrical action starts from this point more readily in disease.

Nobili had tetanized muscle by rapidly interrupting direct current application.[68] Jolly found that if the tetanizing current was applied interruptedly to the orbicularis oculi muscles of a patient with myasthenia gravis "the tetanus becomes less complete after each successive stimulus" until it finally can no longer elicited.[69]

Geigel [70] discovered that compression of the circulation to a nerve resulted in a negation of the Heidenhain-Erb formula (the Rich reaction).[71]

[63] This was announced before the present electrical units were accepted at the Congress of Paris in 1881. His notations of E. M. F. were listed as the number of battery elements; resistance in number of feet of 1 mm. copper wire; amperage in degrees of deflection of the galvanometer needle.

[64] *Loc. cit.*

[65] Mann, L.—Untersuchungen über die elektrische Erregbarkeit im frühen Kindesalter, mit besonderer Beziehung auf die Tetanie. *Monat. f. Psych. u. Neur.*, 1900, v. 7, p. 14.

[66] Erb, W.—*Die Thomsen'sche Krankheit.* Leipzig, 1886, p. 67. Normal excitability of the nerve, galvanic and faradic hyperexcitability of the muscle and the sluggish tonic prolonged contraction which persists after excitation," the sum of all of which manifestations . . . can be called the "myotonic reaction."

[67] Weiss, G.—*Technique d'Électrophysiologie.* Paris, 1895.

[68] Garratt, A.—*Electrophysiology and Electrotherapeutics.* Boston, 1861, p. 83. "By the rapidly repeated closure and opening of the circuit that embraces a frog's thigh, there appears a phenomenon which bears the greatest resemblance to ordinary tetanus."

[69] Jolly, F.—Myasthenia gravis pseudoparalytica. *Berl. Klin. Wochen.*, 1895, v. 32 p. 33.

[70] Geigel, R. and Voit, F.—*Lehrbuch der klinischen Untersuchungs-Methoden.* Stuttgart, 1895, p. 279.

[71] Schiff working on compressed nerves noted that the nerve responded to stimuli above the site of compression thus dissociating the individuality of two nerve properties—excitability and conductivity. Battez showed that stimulation of a traumatized, but continuous nerve, above the lesion would elicit contraction in the supplied muscle (Reaction of Conductibility). Erb had indicated this same effect in 1868.—Zimmern, *op. cit.*, pp 94-105.

Ghilarducci [72] found a point of maximum irritability other than the motor point in nerve degeneration. This had been indicated previously by Remak (1876), Doumer (1891), and Huet (1894) but it remained for Wertheim-Salomonsen [73] to popularize the "displacement of the motor point" as a diagnostic finding.

In 1922 Soderbergh [74] while examining a proven case of Wilson's disease found an unusual response to electrical stimulation which he later called the myodystonic reaction (R. M. D.) and which seems to be of confirmatory value in that disease.

The French speak of that period in electrodiagnosis which first became concerned with the time factor as "modern." Lapicque has been its chief historian and a major contributor. He begins its story by condemning Du Bois-Reymond and his followers for perpetrating the scientific crime of prohibiting others for many years (through the influence of their authority) the correction of the statement made in 1848 that "It is not the absolute value of current-density in the nerve, at any given moment, that determines the response of muscle, but the variations of this value from moment to moment." [75] The satellites of Du Bois-Reymond continued the study of neurophysiology, and it probably occurred to some of them that the master was wrong, but no retraction was published. When one of his pupils, Bezold, dedicated his book [76] to his "teacher and dear friend Du Bois-Reymond," he included the length of the latent period of muscle stimulation but failed to mention "the law" of Du Bois-Reymond.

Fick [77] used an apparatus in which a metal contact point on a stretched rubber-band flew across a supporting plate (under the elastic recoil of release) and thereby closed the circuit. He was able to administer stimuli in hundred-thousandths of a second. He learned that the briskness of stimulus could vary within certain limits and that "The current, to produce excitation must flow a certain length of time." He concluded that, "for the striated muscle of the frog (at least), the law of Du Bois-Reymond is not the last expression of truth." [78]

[72] Ghilarducci, F.—Sur une nouvelle forme de la réaction de dégénerescence. *Arch. d'électr. méd.*, 1896, v. 4, p. 17.

[73] Mann, L.—L'état actuel de l'électrodiagnostic. *Arch. d'élect. méd.*, 1903, v. 11, p. 32.

[74] Soderbergh, G.—The Myodystonic Reaction. *Acta Med. Scand.*, 1922, v. 56, l. 585. "The muscle responded to faradic current normally, but the relaxation was abnormally slow and disconnected."

[75] Biederman, *op. cit.*, p. 116.

[76] Lapicque, L.—*Physiologie Générale du Système Nerveux.* Paris, vol. 5, p. 30.

[77] *Ibid.*, p. 30.

[78] *Ibid.*, p. 32.

In 1867, Brücke showed that nerve and muscle could be excited separately.[79] In 1870, Engelman worked with the ureter muscle of a rabbit which contracts slowly enough to observe easily. He found a regular relationship between intensity and duration of current flow (strength-duration curve) and called the duration factor of stimulation the "physiologic time."[80] König[81] obtained brief stimuli with a pendulum constructed for him by Helmholtz. In spite of the admission that "the electric current must continue to act during a certain time to produce molecular changes in the nervous substance" he found no disagreement with "the law." Lapicque[82] investigated the medical and university politics of the time and indicts Helmholtz for his influence on König, and friendship with Du Bois-Reymond with the lamentation, "Helmholtz sacrificed scientific truth for friendship not ambition."

In 1871 Tiegel[83] suggested the use of condenser discharges as a method of obtaining short lasting stimuli. Two years later Chauveau fashioned condensers from spaced rings of metals for this purpose.[84] Dubois[85] seems to be the first after Engelman to question "the law," but to the Dutch physics teacher, Hoorveg goes the credit of boldly asserting, "I must consider it an effort in vain to save the old classical law . . . nerve excitation is not evoked by changes in the current" . . . but . . . "is a function of the time and intensity."[86] Cybulski and Zanietowski[87] had been paralleling the work of Hoorveg and were quite upset to find that their publication had been ignored. Their results were first published in a Polish journal which did not enjoy an international audience. Perhaps this was fortunate, inasmuch as their conclusions were based on an experimental error resulting from defective wire insulation.[88]

Augustus Waller at first considered stimulation as a quantity of energy but later[89] realizing the importance of the time element, spoke of the

[79] *Ibid.*, p. 34.
[80] *Ibid.*, p. 39.
[81] *Ibid.*, p. 44.
[82] *Ibid.*, p. 46.
[83] Tiegel, F.—*Pflügers Arch.*, 1877, v. 14, p. 330.
[84] Cybulski, N. und Zanietowski, J.—Ueber die Anwendung des Condensators zur Beizung der Nerven und Muskeln statt des Schlittenapparates von Du Bois-Reymond. *Arch. f. d. ges. Physiol.*, 1894, v. 56, p. 45.
[85] Lapicque, *op. cit.*, p. 59.
[86] Hoorveg, J.—Ueber die elektrische Nervenerregung. *Arch. f. d. ges. Physiol.*, 1892, v. 52, p. 87.
[87] Lapicque, *op. cit.*, p. 58.
[88] *Ibid.*, p. 59.
[89] Waller, A.—*Proc. Roy. Soc.*, 1899, v. 45, p. 214. Waller was the first to describe nerve degeneration and with it the one general law of biology—the portion of a cell which is separated from its nucleus, dies.

duration intensity relation as the "optimal minimal stimulus." Lucas carried this work forward by "choosing arbitrarily an increasing series of potentials to which condensers were to be charged and seeking for each potential the minimum capacity which yielded a contraction of muscle." [90] He proposed "to adopt as a label for each excitable substance in tissue the 'excitation time.'" [91]

In 1901 Weiss [92] studied the minimal energy needed to excite. But with the condenser method "one does not know at what moment one can consider the effective discharge as ended." He sought a rectangular wave of excitation and was able to produce one with his ballistic rheotome, which was an ingenious departure from the devices previously introduced.[93] With this instrument he developed a simple but inaccurate excitation formula.[94]

Madame and Louis Lapicque carried on the tradition of experimental neurophysiology at the Sorbonne with Weiss' apparatus, but soon found that a more flexible instrument was needed. Lapicque developed a precision gravity-operated pulley circuit breaker which allowed greater

[90] Lucas, K.—The Excitable Substance in Amphibian Muscles. *J. Physiology*, 1907, v. 36, p. 113.

[91] Lucas found three different strength-duration curves for amphibian muscle. Lapicque later claimed that the strength-duration curves of all tissues would coincide if suitably scaled (isochronism) and suggested three sources of error in the work of Lucas. Rushton could accept only one of these and insisted that "there are two excitabilities, gamma and alpha in the nerve muscle complex of which gamma is isochronous with nerve and alpha has a chronaxy many times longer." Rushton, W.—Normal Presence of Alpha and Gamma Excitability in the Nerve Muscle Complex. *J. Physiology*, 1931, v. 72, p. 265.

[92] Weiss, G.—Recherches sur l'excitation des nerfs par les courants de très courte durée. *Compt. Rend. Soc. Biol.*, 1901, v. 53, p. 253.

[93] The instrument was simple but tedious to operate. For each determination a projectile was fired from a coiled spring through two successive wires. As the bullet cut through the first it closed the circuit, and when it cut through the second it opened it. The distance between the wires could be varied to alter impulse duration.

[94] Davis, H. and Forbes, A.—Chronaxie.—*Physiol. Reviews*, 1936, v. 16, p. 407. These authors collected about forty excitation formulae from the literature. They conclude that "apparently no simple theory or equation can cope with the complexity of electrical excitation, and any simple index of the speed of the excitatory process must either be incomplete and limited in application or be an empirical approximation."

There have also been many theories attempting to explain the origin of muscle contraction, from the electric fluid of Galvani, through the ion concentration of Nernst. In 1920, Loewi found a soluble substance at the vagus terminus following its stimulation, which would stimulate the muscle of another heart, and this led to the concept of humoral transmission of nerve excitation. Kibjakow suggested that acetyl-choline might be the transmitter substance of excitation from one neurone to another.—*Arch. f. d. ges. Physiol.*, 1933, v. 232, p. 432. Marnay accounted for its disappearance by saponification during the refractory phase.—*Compt. Rend. Soc. Biol.*, 1937, v. 125, p. 41.

accuracy.[95] In 1909 he named the threshold "the rheobase," so called because it is the base above which the variation of intensity as a function of time during which the current passes is developed. From the Greek *chronos* for times and *axia* for value, he derived the word *chronaxie* to denote the minimal value of current duration at double the rheobase intensity needed to excite.[96] The concept was not new, but it was the first expression of time and intensity which caught on.

Hoorveg and others had used condenser discharges in man to arrive at an excitation formula. Clüzet used the same method to determine whether Weiss' formula applied to man.[97] He found that the duration of stimulus in health could be as little as .0002 seconds, and that in nerves which had lost their faradic excitability the stimulus needed might be as long as .01 seconds. The notion of stimulus duration led Cluzet to use a variable capacity test apparatus in 1911. At about the same time Doumer [98] was studying the "time constant" in man, and in the following year Bourguinon began the study of chronaxy in man even though Lapicque had assured him that it could not be done.[99]

H. Lewis Jones [100] was the first to report on the value of condenser discharges as a differential diagnostic procedure. He used a battery of condensers with which he was able to achieve "the ready recognition of twelve different degrees of muscle excitability." He was pleased with the

[95] Lapicque, L.—Première approximation d'une loi nouvelle de l'excitation électrique basée sur une conception physique du phénomène. *Compt. Rend. Soc. Biol.*, 1907, v. 1, p. 615.

[96] Lapicque, L.—Définition expérimentale de l'excitabilité. *Compt. Rend. Soc. Biol.*, 1909, v. 67, p. 280.

[97] Cluzet, M. J.—Sur la détermination au moyen des condensateurs de la formule d'excitation d'un nerf ou d'un muscle. *Compt. Rend. Soc. Biol.*, 1907, v. 1, p. 300.

[98] Doumer, E.—*Ann. d'Electrobiol.*, Apr. 1910, p. 21 in Laugier, H.—*Vitesse d'Excitabilité et Courants Induits.* Paris Thèse, 1913, p. 80.

[99] Bourguinon, G.—*La Chronaxie chez l'Homme.* Paris, 1923, p. ii. Among the very many contributions made by Bourguinon to the subject of human chronaxy is the ratio of values for antagonist flexors and extensors which he placed at 1 : 2 or 1 : 3. (Law of Bourguinon) *op. cit.*, p. 170. In 1802 Ritter had discovered that weak stimuli applied to nerve trunks produced movement in one group of functionally co-ordinated muscles—the more excitable, which he found to be the flexors. Rollett in 1874 confirmed this relationship for tetanizing currents.—Biederman, *op. cit.*, p. 96. In 1928 Lapicque claimed that the greater excitability of the flexors was a phenomenon of central control and when present indicated intact nerve pathways (chronaxy of subordination). Interruption of the pathways in the higher levels equalizes flexor and extensor values (chronaxy of constitution). Lapicque, L.—*Quelques Problèmes Généraux Relatifs au Fonctionnement du Système Nerveux.* Paris, 1936, p. 50.

[100] Jones, H. L.—Use of Condenser Discharges in Electrical Testing. *Proc. Roy. Soc. Med.*, 1913, v. 61, p. 49.

diminished pain of this method and its consequent ease of application in children. His apparatus was soon improved by Hernaman-Johnson [101] who varied the voltage as well as the capacity and thus brought the apparatus to the approximate stage which Bourguinon suggested in the same year when he wrote for the first time on chronaxy in man.[102] Through his persistence and energy Bourguinon developed chronaximetry into the most accurate and valuable electrodiagnostic procedure.

Elihu Thompson showed that if the number of waves in an alternating current exceeded a frequency of 10,000 per second, neither sensory nor motor response would be elicited by it.[103] In 1888 Roth used an alternating current of audiofrequency and observed that the threshold potential of muscle excitation rises as the frequency is increased.[104] This was verified by d'Arsonval and more recently by Renqvist [105] who used frequencies up to 40,000 cycles per second and found a minimum threshold for intensity and frequency. Coppée [106] developed the threshold for high frequency stimulating currents which he named "isopotential frequency." As yet high frequency stimulation has not been used diagnostically in the clinic.

Vigoroux [107] found a diminution of skin resistance in patients with exophthalmic goitre and an increase in hysterical patients on the side of anesthesia. He attributed these findings to changes in the superficial circulation and not to the state of the epidermis. Féré [108] placed electrodes of the same diameter on the anterior surface of the forearm and the posterior surface of the thigh and passed a current through them and a

[101] Hernaman-Johnson, F.—The Use of Condensers in the Diagnosis and Prognosis of Nerve Lesions. *Lancet*, 1916, v. 1, p. 351.

[102] Bourguinon, *op. cit.* [103] Weiss, *op. cit.*, p. 184.

[104] Roth, J.—*Pflügers Arch.*, 1888, v. 42, p. 91 in Coppée, *op. cit.* Kronecker in 1868 found that if the frequency of a tetanizing current was sufficiently increased the muscle would respond with a brief jerk instead of tetanus. Wedensky (1883) showed that stimuli sufficient to produce contraction of a muscle indirectly when stimulated through its nerve, may fail when they are repeated at certain relatively rapid rates.

[105] Renqvist, Y. and Koch, H.—*Skand. Arch. f. Physiol.*, 1930, v. 59, p. 279 in Coppée, *op. cit.*

[106] Coppée, G.—Une nouvelle caractéristique chronologique de l'excitabilité. *Arch. internat. de physiol.*, 1934, v. 38, p. 251.

[107] Vigouroux, R.—Sur le rôle de la résistance électrique des tissus dans l'électrodiagnostic. *Compt. Rend. Soc. Biol.*, 1879, v. 31, p. 336. Weil reported a lowered resistance in Grave's disease and neurasthenia, i. e., in conditions with depression of the centers controlling skin humidity; and increased resistance in hysteria. Weil, E.—*Manuel d'Électrothérapie*, Paris, 1916, p. 193.

[108] Féré, C.—Note sur des modifications de la résistance électrique sous l'influence des excitations sensorielles et des émotions. *Compt. Rend. Soc. Biol.*, 1888, v. 5, p. 217.

galvanometer. He noticed a brisk deviation in the indicating needle after visual, auditory, painful and other stimuli. He thought that this verified the hypothesis of decreased skin resistance secondary to increased circulation. Tarchanoff [109] explained the reaction as an active state of the sweat glands which produces a secretory current.

Veraguth [110] named the skin phenomenon "psycho-galvanic reflex," and ruled out the effect of circulation by using an Esmarch bandage, and the perspiration effect by drying the hands with formalin. His subject grasped two nickel-plated cylinders through which a small current was fed. A series galvanometer was read every fifteen seconds. After a period of stabilization (fifteen minutes) emotive and physical stimuli were seen to be followed by fluctuations in the current flow within a few seconds. Peterson [111] found that the size of the current variation depends upon "the liveliness and actuality of the emotion aroused, and that the wide excursions of the recorded waves expressed great emotional lability." The test found its chief diagnostic value in acute catatonic forms of dementia praecox, in which the latent time is greatly increased, and the waves become diminished in size and slope.

Aelby [112] definitely excluded tissue resistance as the basis of the reflex and cited polarization of the skin as the important factor in the production of the reflex.

Waller [113] dropped the prefix "psycho" because it was not a cortical phenomenon, and added that "the more perfectly an examinee can control the visible signs of the emotion, the more violently is the galvanometer deflected." [114] Prideaux [115] has given an excellent summary of the development of the galvanic reflex. From the simple original electrical circuit of Veraguth, the testing equipment has evolved through the Wheatstone bridge arrangement of Waller [116] to the vacuum tube apparatus of Davis.[117]

[109] Prideaux, E.—The Psycho-Galvanic Reflex. *Brain*, 1920, v. 43, p. 51.

[110] Veraguth, Otto—*Das psychogalvanische Reflexphänomen*. Berlin, 1909.

[111] Peterson, F. and Jung, C.—Psycho-Physical Investigation with the Galvanometer. *Brain*, 1907, v. 30, p. 153.

[112] Prideaux, *op. cit.*, p. 57.

[113] Waller, A.—Mensuration de l'émotion nerveuse chez l'homme. *Bull. de l'Acad. Roy. de Méd. de Belgique*, 1919, v. 29, p. 1171.

[114] Waller, A.—Periodic Variations of Conductance of the Palm of the Human Hand. *Proc. Roy. Soc.*, 1919, v. 91, p. 17.

[115] Prideaux, *op. cit.*

[116] Waller, A.—Demonstration of the Psycho-Galvanic Phenomenon. *J. Physiol.*, 1918, v. 52, p. 474, vi.

[117] Davis, R. and Porter, J.—A Measuring Device for the Galvanic Reflex. *J. Gen. Psychol.*, 1931, v. 23, p. 553.

Gildemeister [118] stressed the high counter E. M. F. produced in human skin as a result of the polarization resulting from the passage of galvanic current through it. Since the greater part of the recorded resistance is an artefact of polarization of applied direct current, Brazier [119] avoided this by measuring skin resistance with the alternating current. She disregarded the accepted electrical structure of the human body and considered it as a dielectric. Dielectrics are measured by a specific physical property called the dielectric loss angle, which is independent of the size or shape of the object measured. The dielectric loss angle, or angle of impedance (I. A.) is a measure of a physical property of the human tissues and not of the skin alone. By measuring the impedance angle in many normal and diseased patients, Brazier showed its specific diagnostic value in hyperthyroidism. Unlike the rigid conditions which have to be satisfied in performing a basal metabolic rate determination, the I. A. which is unrelated to the ordinary physiologic and environmental variations can be performed rapidly and in the unprepared patient.

Impairment of sensory nerve function frequently leads to diminution of sweating in the area of its distribution. The resistance to current flow through the skin is a function of its surface moisture. Richter and Katz [120] have been able to map out areas of sensory disturbance by passing a minute current through the skin and a galvanometer, which has proven of considerable value because of its rapidity and independence of patient cooperation.

[118] Gildemeister, M.—Über elektrischen Widerstand, Kapazität and Polarisation der Haut. *Pflügers Arch.*, 1919, v. 176, p. 84. Bordier had recognized the influence of polarization under the testing electrodes and considered the body as a condenser with a capacity estimated at .0025 microfarads. Weil, *op. cit.*, p. 193.

[119] Brazier, M.—Impedance Angle Test for Thyrotoxicosis. *West. J. S., O. G.*, 1935, v. 43, p. 429.

[120] Richter, C. and Katz, D.—Determination of Peripheral Nerve Injuries by the Electrical Skin Resistance Method. *Journal A. M. A.*, 1943, v. 122, p. 648.

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TEXTS AND DOCUMENTS

ON MODERN SYPHILOTHERAPY WITH PARTICULAR REFERENCE TO SALVARSAN

BY

ALBERT NEISSER

(*Sammlung zwangloser Abhandlungen aus dem Gebiete der Dermatologie, der Syphidologie und der Krankheiten des Urogenitalapparates.* . . . Band I, Heft I, 1911). Translated from the Original German by ISABELLE VON SAZENHOFEN WARTENBERG.

BIOGRAPHY AND BIBLIOGRAPHY BY FRANCES TOMLINSON GARDNER*

ALBERT NEISSER (1855-1916)

Those interested in the history of medicine know that the clammy micrococcus of gonorrhea was first dragged from obscurity and presented to an anxious world by a scientist named Neisser. Some people, if prodded, can produce a few other facts about the scientific life of the discoverer. They know that a syringe is named after him, and that certain other coccaceae with added syllables like Neisseria intracellularis and Neisseria lactea are named in his honor. They think perhaps he might have had some connection with Wassermann. They can offer very little information about the man himself. The personality and extra-curricular activities of a useful but unromantic German physician passed unnoticed in a preoccupied world which has had interest only in the scientific crutches with which he propped up its diseased and unsavory substance.

Albert Ludwig Siegmund Neisser was born in 1855 in the town of Sweidnitz near Breslau, the son of Moritz Neisser a distinguished Jewish physician. He had a thorough education in Breslau and Erlangen and took his degree in medicine at Breslau in 1877. His graduation thesis " Die Echinokokkenkrankheit " was thorough, ponderous and scholarly and certainly the work of a young man who had a future. So thought Oscar Simon, chief of the Royal Dermatological University Clinic at Breslau. He asked the young man, in whom he though he saw a bud of genius, to be assistant in his clinic and worker in his laboratory.

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The arrangement was not one for a lazy man for the clinic was large. Skin diseases were still hideously prevalent in the last half of the nineteenth century, and were only dimly understood. Venereal diseases were uncomprehended. Their hidden origins kept them safe from exploration and treatment until such time as man might happen on some instrument which would penetrate their invisibility. Neisser, student of Heidenhain, Cohnheim, Weigert, Koch and Ehrlich, was as sensitive to the possibilities of the microscope as a pianist to his keyboard. He was young, fresh, curious and confident.

Breslau was celebrated for its clinic, and patients came painfully from great distances to get what information they could from its learned staff. The percentage of luetics was high, and the victims of gonorrhea hobbled in and hobbled out, not greatly benefited by the treatment given them. Young Neisser watched and worked. It was not a secret that something microscopic was the cause of gonorrhea, and of syphilis too. It was merely that no combination of stain and method had yet cornered either. Neisser knew that wise old heads had searched unsuccessfully ever since the microscope had enjoyed any potency at all. He, at twenty-two, was entirely undismayed by such competition. His microscope stood beside those of Breslau's scholars in Simon's clinic, and as one after another discarded slide after slide and theory after theory, he went on, quietly and unobtrusively, with his own hunt.

With the solid stolid persistence which was characteristic of him, Neisser stained and peered and discarded mountains of slides. He burned a lake of midnight oil. Whenever he could steal a moment from an itching and tormented patient, he spent it recklessly in the laboratory. He was deaf to comment, argument or discouragement. Perhaps his very persistence appealed to Providence for she rewarded him early, as time goes for that sort of thing. In 1879, only two years after he had begun, Neisser found his villain. Under high power illumination on a slide prepared by Koch's method, swimming in a watery solution of methyl violet, frolicked the evil one. Although it was found in gonorrheal pus and although Neisser was as sure of it as he was that his own head was where it should be, he did not name it gonococcus at that time. His first paper of exposition refers to it only as a " micrococcus." Not until 1882, after many examinations and experiments in a most conscientious way, did he finally christen it as " gonococcus."

At twenty-four Albert Neisser became a personage. As time passed he developed an enormous private practice from which he grew wealthy. He was of a temperament, however, which could not be satisfied by days

filled with the complaints of single individuals. He must have research to complete his life. His interest in gonorrhea continued until he was called "the father of the gonococcus" and recognized throughout the world as a pioneer in the rational treatment of the disease. In an age of scoffers he insisted on constant control by microscope, nonsense to most contemporary practitioners. He fought bitterly against the common inclination to use astringents to the exclusion of every other type of medication and was the first to recommend the use of protargol.

Neisser's early career and its extraordinary climax led inevitably to a series of anti-climaxes. All his achievement in later life was not enough to surpass that which he accomplished as a mere boy. Had it been otherwise, the stature of the man would have been defined more clearly. He was a great crusader and a versatile performer. In the years between 1879 and 1912 he had his hand in many a kettle of fish, both hot and cold. He travelled Europe from end to end urging the establishment of clinics for skin and venereal patients which would be set apart from clinics open to other diseases. He begged for more clinics in universities. In spite of the soundness of his theories it was years before anyone would listen to him. He became head of the Polyclinic on the death of Simon in 1882 and ever after clung to his position there. He would not budge, even for an offer to succeed Lewin in Berlin in 1896. Breslau belonged to him and he to Breslau. One by one he added to his activities the direction of research in biology, histology, protozoology, bacteriology, x-ray and the Finsen light. He became concerned with leprosy, spent much time in Norway and Spain in the study of it and finally confirmed and extended much of Hanson's work on the leprosy bacillus.

Just before the turn of the century the battle against syphilis began to accelerate. Virchow, Fournier, Unna and Hutchinson contributed valuable ammunition. As the new century dawned all bacteriologists were eying the efforts which were then being made to transmit syphilis to some one of the lower animals so that it could be studied. All the candidates stubbornly refused to be infected. Neisser, with many others, was making his own experiments. In an ecstacy of zeal one day, he inoculated four perfectly healthy and presumably amenable human subjects with syphilis, somewhat in the Hunterian tradition. For this operation he was publically reprimanded by the authorities, and fined. Nothing was ever heard further from the experiment. Perhaps the inoculation did not take. Perhaps the subjects were cured later when Ehrlich developed 606.

In 1903 Metchnikoff and Roux succeeded in producing syphilis in apes. This success can not be overestimated, for it marks the first time that

syphilis could be studied from inoculation to termination. Immediately Neisser became enthusiastic. He built a monkey house in his backyard and filled it with 200 shrieking boarders to the dispair of his wife and the entertainment of his adopted son. In his simian martyrs he began to sow the seeds of venereal woe. The martyrs accepted their discomfort stoically, but were less cheerful about the effects of the north German climate. Within two years it was obvious that a backyard in Breslau was not the place to raise monkeys, and Neisser gave what he had left to the University laboratories. Undismayed, he packed himself, his wife and two assistants into a steamer and went all the way to Java, where he had been assured he would find a plethora of healthy and cooperative monkeys. In this tropical paradise he discovered the spirochaeta pallida, the cause of syphilis. Unfortunately for his own fame, Fritz Schaudinn and Eric Hoffmann, working quietly at home in Germany, had done the same thing and announced their discovery some time ahead of him.

Neisser returned from Java in 1906, and in 1907 joined Bruck and Wassermann in the research which ended in the production of what is known now as the Wassermann test for syphilis. This application of the serum-complement reaction of Bordet and Gengou to the diagnosis of syphilis, marked the beginning of the modern concept of the diagnosis and treatment of the scourge. Neisser, hovering in the immediate background, was part of the drama from start to finish, and in 1909 when Ehrlich triumphantly produced 606, Neisser was immediately at work with it.

The hitherto untranslated paper which is presented here is one of the first which was based on reasonably extensive use of Ehrlich's famous 606. Neisser was aware of the pitfalls which lurked in the careless use of it and appreciated, though he did not understand, "the curiosity" of evident allergic reactions on the part of the hypersensitive patients. Over and over he sounded the warning, so commonly ignored until too recently, that treatment immediately upon discovery of the disease and treatment long and conscientiously continued is the only assurance of cure.

The work with Ehrlich was the last great opportunity of Neisser's life. Though he was only fifty, his health was leaving him. In 1912, while on an excursion into his own cellar, he fell and fractured his hip. During a very protracted recovery from this injury a whole chain of other symptoms and discomforts were visited upon him. Several severe bouts of renal colic disclosed the fact that he was cursed with cystitis and many kidney stones. Evidence was present also which told him and his doctors that, in addition to everything else, he was a diabetic.

In those pre-insulin days, the life of a diabetic was a short and hungry one. Neisser, limping because of his hip, hungry because of his diabetes and in pain because of his stones, carried on as well as he could. In 1916 he went to the occupied city of Brussels to a scientific congress which was being held there in spite of a world at war. On his return he rested only a few days before attempting to go to Dusseldorf for attendance at another congress. This time he only reached Berlin. There he was forced to give up and retire to a hospital. Diabetic or no diabetic, the stones had to come out.

Neisser himself was a doctor. He knew his own condition. He knew that his scant chances of recovery depended upon care, nursing, rest and quiet. Yet, because he was not in Breslau he would not rest or accept the nursing. Nothing would do but that two days after his operation he must have himself carried home to Breslau. There, nature, startled by such mistreatment of a diabetic body, retaliated as might have been expected. He reached Breslau alive, but sepsis had begun. The next day he was in the coma, in which he died on July 30, 1916. Swallowed up in other news, his passing was unnoticed by a warring world.

It was Neisser's fate to perform too well too soon, and forever after to be the shadow hovering near the new discovery or treatment which shook the world; to lecture in company with Wassermann and others, and have it said by the listeners "Neisser spoke well too." Yet, he was sound and thorough and a scientist to his finger tips. He should belong as truly to the scientific ages as do the men he honored in his own paper: Schaudinn, Hoffmann, Metchnikoff, Roux, Wassermann, Bruck and Paul Ehrlich.

ON MODERN SYPHILOTHERAPY WITH PARTICULAR REFERENCE TO SALVARSAN[1]

BY

A. NEISSER

Gentlemen:

European physicians have known syphilis for more than four centuries, and for almost as long scientific medicine has been using mercury in its treatment. Yet only the last eight years have improved our knowledge of the nature and pathology of the disease sufficiently so that we are able to replace a purely empirical and therefore uncertain treatment with a rational therapy; a therapy, the principles of which are based not merely upon hypotheses and theoretical speculations, but on actual observations. Seldom indeed has there been such notable progress in any branch of medicine in such a short time as we now note in syphilology. Best of all, these discoveries have been applied directly to the cure of the patient, the highest goal of any medical research. It is important and gratifying that these extraordinary achievements, with all their still-unexplained and unforeseen potentialities, have been attained neither by chance nor by crude empiricism. On the contrary, modern syphilotherapy is the result of exhaustive research in the spheres of etiology, diagnosis and experimental pathology and therapy.

Three great discoveries are the foundation of modern syphilotherapy:

(1) The discovery of the Spirochaeta pallida by Schaudinn with the cooperation of E. Hoffmann. Until recently experimental inoculation with syphilis, which provides the final proof that the Spirochaeta pallida is the cause of the disease, has been impossible. Now the experiments of Sowade of the Grouven's Clinic and those of Noguchi and von Hoffmann (Berlin) have accomplished this conclusively. Since the invariable finding is that the typical spirochete appears in all syphilitic lesions and conditions, we have no doubt that the spirochete is guilty. It is true that diagnosis is made very difficult by the fact that it is not easy to distinguish this spirochete from similar but innocent spirochetes. This however,

[1] Neisser, A. Über Moderne Syphilistherapie mit Besonderer Berücksichtigung des Salvarsans. 1911, 46 pp.

does not affect the fact that the Spirochaeta pallida causes syphilis. That question may be considered settled.

It may be added that the identity of the Spirochaeta may be determined more surely by staining the dry preparation than by using the more convenient and quicker examination in the dark field and the India-Ink method of Burri.

(2) The discovery by Metchnikoff and Roux, that syphilis is transmissible to monkeys. By this discovery the old theory that syphilis is exclusively a human disease, inaccessible to experiment, has been destroyed. At last it has become possible to study experimentally many problems of the pathology and therapy of syphilis. Research work in the field undoubtedly will become more successful as time goes on. Bertarelli, and later Levaditi, Uhlenhuth, Grouven, Pürckhauer, Tomaczewski and others have succeeded in showing that not only apes, which are difficult to procure, but also rabbits are very well suited to experimental studies of syphilis. I myself devoted two years in Batavia to this work. The detailed report was published a short time ago.[2]

(3) The adaptation to syphilis examination of the serodiagnostic method of Bordet and Gengou by A. von Wassermann and his co-workers, A. Neisser and C. Bruck. I do not hesitate to state that serodiagnosis is the most important step of all. However, the reaction is so complicated that, according to my experience in more than 35,000 examinations, it should be carried out in a large laboratory having a quantity of material daily available to research workers trained in biology. Both seem to me to be absolutely essential since even an experienced person can make mistakes if he examines only a few sera at a time. These mistakes can easily be avoided by those who examine simultaneously a great number of blood specimens and antigen extracts. For this reason, in my opinion, it is out of the question that the test can be performed satisfactorily in the office of the general practitioner. It seems inadvisable to make the various reagents available for the doctor and thus enable him to attempt the test himself. In my

[2] *Beiträge zur Pathologie und Therapie der Syphilis*, herausgegeben von Albert Neisser, Verlag. Jul. Springer, Berlin, 1911; simultaneously published as Band 37 of *Arbeiten aus dem Kaiserl. Gesundheitsamt* with the title "Bericht über die unter finanzieller Beihilfe des Deutschen Reiches während der Jahre 1905-1909 in Batavia and Breslau ausgeführten Arbeiten zur Erforschung der Syphilis."

Clinic not only are the tests carried out with different titrated antigens according to both the original method and Stern's modification (active examination), but also invariably at least fifty sera are examined at the same time. In this way errors which may arise from failure or abnormality of an individual reaction cannot be overlooked.

What has medicine gained through these three discoveries and the increased knowledge of syphilis?

(1) Experimental (and serodiagnostic) work on monkeys has made it seem more probable to me that without specific treatment a real cure for syphilis can be achieved only rarely if at all. It happens so seldom that we as practitioners can never count on the realization of such a hope. Every case of syphilis must, therefore, be treated by the most energetic methods.

(2) Through extensive experimentation in Batavia I have been able to demonstrate that our former theory, that immunity can be established by a positive cure of syphilis, is without foundation. On the contrary, only while syphilis is still active is there immunity of a sort; that is, resistance to a reinfection. Even the old theory of absolute insusceptibility to a new inoculation during an acute stage of syphilis can be supported no longer. However, I do not go as far as Finger, Ehrmann and others who consider the occurrence of superinfections as something quite usual. On the whole I think we should assume that, especially during the first years of illness, there exists a high degree of resistance to new infection.

On the other hand superinfection by autoinfection or by foreign viruses are easily possible during the first weeks *post infectionem* as long as no general " constitutional " infection of the whole body-organism, or especially the epidermis, has taken place. When superinfections occur we speak of " multiple successive chancre." In later stages when syphilis has slowly lost its character as a constitutional disease new exposures may be effective and produce such changes as constitute a primary lesion, remaining locally limited or spreading to produce general disease. Therefore it may be unimportant whether the first infection, still present, appears through an evident tertiary focus or stays latent. Practical experience proves the error of the old theory that a syphilitic or a cured syphilitic can heedlessly expose himself to new dangers of infection.

Reinfection has been known for a long time. The reason for its comparative rarity is that complete cures have occurred very seldom. I am convinced that in the future we will see multiple infections much more frequently, since by modern therapy it may be possible to cure our patients quickly of their primary disease.

Unfortunately our investigations have shown also that at present no form of active or passive immunization is artificially produced. There probably never will be any. Our extensive experiments in this direction, which were carried out in Batavia, lead to no positive result. The data available in the literature does not seem to give conclusive evidence that we have any reliable method of immunization.

It is true that Kraus and Spitzer recommend actively immunizing luetics in their primary stage with an emulsion of primary lesions containing killed syphilis virus. After this treatment they have observed the absence of secondary symptoms as well as a a negative reaction and therefore believe that syphilis can be arrested through immunization; that is, the spread of infection throughout the whole body can be prevented. As far as these assertions have been examined it has not been possible to confirm them. (Neisser, Brandweiner, Kreibich). Nevertheless the results, especially the latest reported by Spitzer, based on repeated serological examination of cases in which pure infection was observed, are so remarkable that the field seems to warrant further research.

For the present we most emphatically stress the need for and the importance of chemotherapy, which has employed mercury for several centuries and which recently has adopted the use of arsenic preparations.

(3) Treatment has been given indirect assistance through the improvement of our diagnostic procedures principally in regard to the following points:

(a) Demonstration of the Spirochaeta often permits a diagnosis of a very early infection, something in which our clinical methods of examination have failed heretofore. We are now in a position to diagnose erosions and similar symptoms as primary syphilitic lesions.

(b) Serum diagnosis makes detection possible in cases and stages of the disease in which all other methods of clinical examination fail. I need not stress the importance of the achievement. We all know the difficulties which formerly confronted us when facing the question: is

the patient definitely cured or is this only a latent state of the disease? Now we are frequently in a position to give a definite opinion of the absence of symptoms in a particular case. *I am quite convinced that the positive reaction is certain evidence of syphilitic disease, an indication of a still-existing spirochaetal infection in the body.*

In every case with a decided positive reaction there is the possibility of relapse in some form, either tertiary or metasyphilitic. All these cases must be treated. Consequently we now treat patients whom formerly we did not suspect of the disease, or whom we were no longer treating because we were uncertain that infection still existed. Finally, we treat cases which once were not thought to be syphilitic at all, cases in which one was completely at a loss because of missing the "anamnestic reaction" and other pertinent findings.

Serum diagnosis is, therefore, indispensable to the judgment of all asymptomatic cases of syphilis. Only this can help in the difficult determination of how long one should continue the treatment in order to free the patient completely from the virus existing in his body. For that reason I cannot understand why physicians still make so little use of its powerful assistance. It is imperative that a serological examination should be done if there is the slightest suspicion that the appearance of illness might have a connection with a known or an unknown syphilis. Only thus can one trace hidden cases and make a cure possible and at the same time provide a prophylaxis for the particularly disastrous parasyphilitic diseases.

(4) A direct and immediate advantage to treatment is the opportunity to study with precision the effect of certain remedies and therapeutic procedures. There are various methods available for this purpose.

(a) We can determine the action of the spirochetes, their number and their nature in separate local processes, before and after treatment, and control accordingly the effect of certain remedies introduced into the animal body.

(b) We are in a position to determine, through experimental tests, the true disease status of previously infected animals and, for those who are symptom-free, can discount totally valueless clinical observation.

We can either kill the animal and use its organs to transmit inoculation and thus determine if there is any virus present, or we can reinoculate such an animal. If a new primary lesion appears there is a certainty that the animal has been cured of its first infection. If

a single or repeated reinoculation reacts negatively we know that the animal is still sick, that either the treatment or the remedy was insufficient to secure a complete cure.

(c) In the case of a human patient on whom experimentation naturally is excluded, we establish a clear picture of an accomplished cure. A positive reaction must, according to our present day knowledge, be interpreted as a still-existing infection.

To explain the negative reaction is not so easy. I consider it absolutely wrong if, as happens rather frequently, no importance is attached to this phenomenon.

If we wish to consider how therapeutic knowledge has developed on the foundation just discussed, we must contemplate the questions of general treatment on one hand, and the progress of specific therapy on the other.

In the matter of general treatment it is most encouraging that the necessity to begin to treat a syphilitic as soon as possible and to continue treatment until he is infection-free, is now generally recognized. Many, including myself, have known it since 1881. For decades there was a dispute as to whether one should begin treatment as soon as possible after establishing the diagnosis or wait until the full development of the disease in its general secondary manifestations. I have always maintained the first point of view because I never could understand why it should be necessary to let the virus multiply enormously before attempting to destroy it. Now it has been proven, by animal experimentation, that the sooner one begins treatment following infection, the more certain and easy is victory. In syphilis the experimental technique is not easy, but we must remember the related trypanosome and Spirillum diseases, in which, also, the delay of one day decides sometimes whether the animal may be quickly and surely cured, or must succumb to the infection.

It also has been found by experiment that if complete cure is not achieved with the first treatment, that is if a relapse should occur, one must administer a much larger dose in order to cure the relapse—always provided that a cure is possible at all.

The justification for using the information gained by experimentation on animals for the treatment of human syphilis is derived from serodiagnostic findings obtained in the human patient. It has been proven that during the time immediately following infection it is comparatively easy to change a positive reaction into a negative one by correct treatment. We observe, however, that if the disease has become chronic, negative reactions sometimes can be achieved only after the most intensive treatment. Sometimes they can not be obtained at all. There are cases which

I myself have treated in vain in which the reactions remain positive despite all efforts. This is probably due to the fact that there may be encysted foci of spirochetes which cannot be reached by the drug, particularly since we lack reliable methods to stimulate those foci and render them accessible to the drugs circulating through the body in the bloodstream.

It also may be possible that the spirochetes have a phase of latent development or pause analagous to that of the spores and granular forms of some microbes, during which they are less easily attacked by drugs. (Pollitzer and others.)

It is possible also that the relapse-parasites may become immune to poison. This too makes very intensive early treatment necessary. We must confess that we know nothing positive of how syphilis parasites behave in such a case, but the possibility of an acquired immunity against mercury and arsenic in spirochetes cannot be overlooked.

All these things point clearly to the need for energetic treatment in the period immediately following infection. At this time we are most certain of avoiding, by prophylactic and absortive therapy, the continued development and wide spread metastasis of the virus: that is, to achieve what Ehrlich justly called "the ideal of therapeutics, the *Therapia sterilisans magna.*"

AS PRACTITIONERS WHEN SHOULD WE START TREATMENT? THE SOONER THE BETTER

That means as soon as the diagnosis "primary syphilitic infection" can be made either clinically (by the character of the focus of the disease, by anamnesis and the course), or by the demonstration of the Spirochaetae and by serodiagnosis. There is no doubt that in this task, demonstration of the spirochete, presents the most successful means of examination for it leads most often to the earliest diagnosis. Today we are able to go one important step further. We can start treatment of urgent cases (such as engaged and married couples) at once if there is a suspicion of syphilitic infection. If the disease is actually syphilis, such procedure offers the greatest chance for instant eradication. Scientifically the justification for such proceeding is based on the following:

1: I have been able to prove by numerous experiments on monkeys that usually long before the appearance of any primary lesions at the site of infection the general spreading of the poison through the whole body has taken place. This has been uniformly the experience in primary infections wherever

clinical diagnosis has been possible. Everything points to the fact that conditions for general spread are just as, if not more, unfavorable for man than for monkey. To wait for the unmistakable development of the primary lesion means always to lose time, during the period, moreover, which is most valuable for therapeutic success.

2: All therapeutic experiments on trypanosome diseases, Spirilla infections and syphilis in animals have proven that an eradicative treatment of the disease in its incipient stage secures a much easier and more reliable cure than does the treatment of an already developed infection.

Even though there is obscurity in the clinical diagnosis, serodiagnosis allows us to comprehend, at the moment when treatment is recommended, the possible absence of syphilitic symptoms over a period of two to ten years following a doubtful infection. We know whether the absence of symptoms means a latent period (which would indicate the continuation of treatment) or a definite absence of the disease. In the latter case it is not clear, though quite important to the patient, whether his being syphilis-free and remaining so is due to the introduction of the abortive treatment or to the fact that the original infection was not syphilis. However, after all, the main thing is that the person in question is free of syphilis.

WHAT ARE THE MOST SUITABLE METHODS AND DRUGS FOR THE INTENDED PROPHYLACTIC-ERADICATIVE TREATMENT?

1. First of all Metchnikoff's suggested treatment must be mentioned. This is to cause instant destruction of spirochetes which may have entered at the site of infection by disinfection with a 33% calomel salve. With this method it is frequently, unfortunately not always, possible to prevent the development of the disease. We in Batavia and later Siebert of my clinic thoroughly studied this question experimentally in vitro as well as in animals. We recommend a more efficacious salve[3] containing a 0.3% mercuric chloride instead of calomel salve.

[3] The salve contains sublimate 0.3 parts; sodium chloride, 1.0; tragacanth 2.0 amyl alcohol, 4.0; gelatine 0.7; alcohol 25.0; glycerine 17.0; water q.s. 100.0. The chemical factory, formerly H. Byk, Charlottenburg, took over the manufacturing of the salve, since uniform production of it is rather difficult and the necessary consistency depends very much upon the quality of the material used therein. This salve is put on the market under the name of "*Neisser-Siebertsche Desinfektionssalbe.*" A detailed description of the experiment is given in *Jahreskursen für ärztliche Fortbildung*, 1910, v. 4 p. 15. "The results of the newest syphilis research in their importance to medical practice," other references: Siebert, Experimentelle Untersuchung und praktische Vorschläge zur persönlichen Syphilisprophylaxe in Neisser, *Beiträge zur Pathologie und Therapie der Syphilis*, Berlin, 1911, Julius Springer, p. 545.

2. Excision must be considered, as must all mechanical, chemical and other expedients which might destroy the focus of infection. The results achieved so far in human beings have not been very satisfactory. Nevertheless our aim must be to try to carry out these local measures in every case in which it is possible to do so without the destruction of important tissues.

3. Spirocheticidal injections into the area of the seat of infection and into the surrounding lymph passages have been suggested. Hallopeau, Duhot and others are said to have achieved excellent results with them. I have had no personal experience with them. All such experiments on monkeys have failed.

4. As already stated the most important thing seems to be to start as quickly as possible with a suitable general treatment, because we must consider that in man a general contamination of the whole body may take place quickly after an infection, even, perhaps, via the blood stream, at the very moment of infection.

With what remedy shall we carry out the general treatment? Here must be mentioned the great debt which specific therapy owes to experimental research. Only this has made possible the exact knowledge of the efficacy of the old and trustworthy remedies as well as the examination of new ones.

a. I have been able to prove that mercury is a spirocheticide and therefore a specific remedy for syphilis, not merely a symptom-removing drug. Mercury cures not only monkeys afflicted with evident symptoms of the disease but also other animals whose organisms, though they show no recognizable pathological processes, presumably contain the spirochaetae. The endless dispute about the utility of mercury during a latent period is herewith settled in the affirmative.

b. I have been able to prove that the iodine compounds also have therapeutic efficacy, though in a much less degree.

c. The greatest improvement is that many organic arsenical compounds have been found to have a specific therapeutic efficiency in regard to syphilis. Ulenhuth took the first important step in proving the therapeutic value of atoxyl against the spirillosis of chickens. He, with Hoffmann, was the first to publish experiments pertaining to syphilis. I was able to verify these results immediately after Ulenhuth's publications since I had made the same experiments on a large scale in Batavia independently.

The further successful development of arsenic therapy we owe to Ehrlich. He was the first to recognize the chemical constitution of atoxyl thus making possible the production of other organic arsenical preparations. It was Ehrlich alone who discovered the difference between the pentavalent saturated and therefore therapeutically inferior and the super-efficient trivalent non-saturated arsenic combinations. Ehrlich was the first to state the importance of study of the effects of combining various chemical groups with trivalent arsenic. On the basis of innumerable observations on animals afflicted with trypanosome infections and spirillosis he established a chemotherapy based upon definite laws of synthetic chemistry.

The climax of this chemical and experimental research in animals was the discovery of arsenophenylglycine (418) and dioxydiamidoarsenobenzol (606) under the trade mark of salvarsan. I hope that you will bear with me if I forgo at this time, a detailed description of the experiments on animals by Ehrlich and Hata which preceded the therapeutic use of the chemicals. It is enough to say that Ehrlich [4] recognized the trivalent-arsenic compound as the chemical most powerfully lethal for Spirilla and spirochetes and the most effective one for the treatment of animal and man. Thus we have at our disposal an immensely effective arsenical remedy and at the same time the discovery has shown the importance of the synthesis of new preparations and the direction which such synthetic-chemical work should pursue. In fact, studies on organic mercury preparations [5] for the treatment of syphilis which are already under way are encouraging.

I come now to the question of the management of general treatment and that of the utility of salvarsan, which is of paramount interest. I am not concerned whether mercury or salvarsan is the better remedy, but I am happy to know that now we have a second remedy in arsenobenzol (and perhaps even a third in arsenophenylglycine), besides the excellent mercury. (It is ridiculous that often physicians as well as laymen forget how marvellous the therapeutic efficacy of mercury can be). Now we can proceed to the longed-for cure in many cases in which it was formerly impossible because mercury, the sole remedy, failed or could not be applied.

[4] Ehrlich-Hata: Die experimentelle Chemotherapie der Spirillosen (Syphilis, Rückfallfieber, Hühnerspirillose, Framboesie), Berlin, 1910. Julius Springer.

[5] W. Schöller und W. Schraut: Zur Synthese des Asurol. *Therapeutische Monatshefte*, Dezember, 1909. Franz Müller, Walter Schoeller und Walter Schraut: Zur Pharmakologie organischer Quecksilberverbindungen. Ein Beitrag zur Wirkung der Metallgifte. *Biochemische Zeitschrift*, 1911, 33. Band, 5. und 6. Heft.

I believe, moreover, that arsenobenzol is in many respects superior to mercury because it promptly and effectively kills the spirochetes. It is, therefore, especially suited for use in abortive treatment. We should treat every new case of syphilis, even every suspected case, with "606," as promptly and as energetically as possible. Perhaps I had better say "also with '606.'" Personally I repeat the injection two or three times because I do not rely on the complete success of one single injection (at least not in doses up to 0.6). Almost always I add an intensive mercury treatment (in the form of grey oil and Asurol injection).

To publicize these cures and acquaint physician and layman with the necessity for them seems to me to be our most important duty if we are to help the individual patient and also to fight against syphilis as a public disease. The abortive treatment is all the more important since we are convinced that the most dreaded consequences of syphilis, tabes, paralysis and aortic changes can only be brought to a standstill and can never be cured completely even with arsenobenzol. Our urgent task is to prevent the development of these sequelae. With this in mind we must act as early as possible because to date we are ignorant whether or not the beginnings of these degenerative processes start soon *post infectionem*. Furthermore, arsenobenzol, because of its powerful spirillicidal properties and its rapid attack on primary and secondary manifestations is of first importance in the elimination of the danger of contagion. Even if relapses occur after a cure with salvarsan, in most cases they are so isolated and localized that they are not as dangerous as those occurring otherwise.

Apparently, besides this direct spirillicidal efficacy, salvarsan causes secondary indirect damage to the spirochetes. It seems (1) that the normal antibodies of the host are produced in increased numbers and (2) that through the destruction of the spirochetes by the salvarsan a healing substance of a presumably antitoxic nature is formed. This substance contributes to the healing of the disease processes. The injections of serum obtained from syphilitics treated with "606," or from the milk of mothers or wet nurses treated with the drug show sometimes a surprisingly favorable influence in producing the retrogression of symptoms and improvement of the general state of health, especially when given to congenitally syphilitic children. It has not been established whether any part is played in this situation by arsenobenzol or arsenic which may have passed into the milk or serum.

The fact that we are able to eliminate contagion more quickly and conveniently than heretofore—often, indeed, by one single injection and by a treatment requiring but a few days—seems to me almost the most im-

portant fact in Ehrlich's discovery. With skillful application of the treatment a decline of syphilis through decreasing sources of infection is bound to result. The hope is justified that the brevity and convenience of the treatment will cause people who hitherto remained untreated to accept it. Now these people can be rendered harmless to their community. The stay in the hospital will become shorter and the cost of treatment will become less. We are even justified in hoping that prostitution, the main source of syphilitic disease, will be robbed of its dangers.

Furthermore, the faster healing process must be considered in all luetic infections of the vital organs, especially in the severe forms of malign syphilis, such as syphilis of the brain or of the organs of sense. This is true also in the major ulcerous developments which may lead to irreparable destruction, as in severe ulcerous lues of the mucous membrane—the nose for example.

Presumably the healing of ulcerous conditions can be explained not only as a result of the destruction of the virus but also by the action of the drug as an organotrope. Too, salvarsan has definite antitoxic effects. The surprisingly quick subsidence of pain and extreme discomfort, often within a few hours, cannot be explained satisfactorily as a result of the destruction of the spirochetes.

Salvarsan can be substituted for mercury:

1. In cases of idiosyncrasy to mercury, especially in cases in which treatment cannot be postponed because of the dangerous condition of the patient and in which there is no time for the patient to get used to mercury.
2. In cases which do not react well or do not react at all to mercury.
3. In cases of severe paronychia, leukoplakia and similar conditions where mercury apparently fails, while excellent results are often achieved with "606" (or arsenophenylglycine).
4. In cases in which, because of an existing sensitivity of the intestines or the kidneys, or because of other organic disturbance, mercury therapy should be avoided. According to experience to date salvarsan is certainly less damaging than mercury to the organs of the body, especially to kidneys and intestines. The very annoying stomatitis may be avoided.

Many, especially general practitioners, will perhaps disagree with this and tell me that among hundreds of mercury treatments they never encountered a poor result. But how effective were those mercury cures?

Did those doctors really achieve what they set out to do? Where then, does the army of aneurysms and of aortic diseases, of tabes patients, of paralytics and tertiary syphilitics come from? Whence arises the shortening of life for a very large percentage of syphilitics? Certainly nothing is easier and more convenient for the physician as well as the patient than harmless mercury treatments. Unfortunately the picture is entirely different if one examines the really vigorous mercury cures. There we find so many unavoidable immediate and delayed effects that I am very glad in some cases for the chance to dispense with the application of mercury entirely or at least to mitigate it by using "606."

The particular nerve-damaging effect attributed to "606" seems to me to be undemonstrated. I am inclined to the belief that nearly all cases described as damage to the nerves of sense caused by "606" should be called "neurorecidive," that is, due to the actual development of lues, even if—and it is not yet proven—there seems to be a special connection between the effect of "606" and the formation of these "neurorecidives." From the beginning salvarsan should be acquitted of the accusation that it is the cause of disease of auditory, optic, oculomotor or facial nerves. This is a condition unmasked but not caused by "606." Such diseases of the nerves have always been known, but formerly one was not particularly concerned about them, and did not pay any particular attention to them. Of course they occur today as in former days before the use of salvarsan. In one week I observed one syphilitic disorder of the auditory nerve and three cases of herpes zoster in syphilitics untreated by "606" (in comparison with two cases of herpes zoster following treatment). If this syphilitic with his rightsided deafness had come into our hands four weeks sooner he would have been treated with "606" and the number of our unsuccessful cases attributed to salvarsan would have been wrongly increased by one.

Formerly many such cases were diagnosed as not being syphilitic sequelae. This was because the connection between syphilis and such nerve involvements was not realized. Today the number of syphilitics undergoing treatment has certainly increased, and all cases treated with salvarsan in which such complications appear are noticed and described. It should not be contested that there may be more cases of cranial nerve injury since the introduction of salvarsan therapy, but an uncontroversial explanation of this increase cannot be given. In view of the therapeutic success achieved through energetic treatment with mercury or "606," in no circumstance can one speak of a purely toxic nerve damage. All experience seems to indicate that when such symptoms occur one should

proceed as quickly and as energetically as possible with just those remedies. The contention that salvarsan by being particularly a "neurotrope" causes a toxic condition of the nerves and thus prepares the ground for a localization of spirochetes in those nerves is clinically and experimentally without foundation.

The well-known "local reactions" (Jarisch-Herxheimer) may become more important. These occur after mercury as well as after the use of "606" but more frequently, it is true, in the latter case when the dose is comparatively huge and is passed suddenly into the body in high concentration. The significance of the appearance of these inflammatory processes accompanied by swellings and redness cannot as yet be interpreted with certainty. Ehrlich explains it as an augmented secretion of toxins from spirochetes still alive and stimulated by the therapeutic agent. Thalmann explains it as the influence of endotoxins liberated from the bodies of spirochetes, the result of aggravation of the syphilitic process.

If such reactions appear on the skin or mucous membranes, they seem rather insignificant to the patient himself. If, however, they are manifested in foci of disease located, for instance, on the periosteum, nerves or brain vessels, the local inflammatory swellings and the pressure and irritation they cause may lead to very disturbing and even dangerous developments such as increased pain in tabes, paralytic symptoms in nerves, epileptic seizures, symptoms of meningitis and so on. Following salvarsan injections one may observe outbreaks of disseminated or isolated foci in locations which, up to that time, had not been the seats of syphilis foci or were not recognized as such and therefore were not diagnosed. It is questionable whether one should interpret such new symptoms as a reaction of hitherto clinically-latent localizations of disease foci or as newly-provoked foci of disease. I am inclined to assume the first hypothesis.

Perhaps we have a neuritis arising in nerves already infected with syphilis, a phenomenon analagous to a local inflammatory reaction. It may be that we have inflammatory reactions of the periosteum of the bone canals causing pressure palsies in the nerves which pass through these canals.

Here may be noticed the principal contrast between irreparable primary nerve-degenerations caused by groups of atoxyls, and changes which appear following the use of salvarsan and are of a reparable and healing nature followed at most by secondary degeneration. I want to state especially that optic nerve atrophy caused by "606" has not been observed. Wherever this has occurred, or has spread, in spite of treatment, it has been explained by the complicated symptoms of the illness.

In short I am convinced that in cases of "neurorecidives" a localization has pre-existed in the particular nerve or in its surroundings (bones, meninges, etc.) whenever such neuro-processes develop during or after "606" treatment. Judging by what we know about relapses in later periods of lues, we can assume that very often these early localizations would have appeared eventually as tertiary nervous affections unless prevented by an especially effective therapy.

We have never seen a case of auditory-nerve involvement in spite of the most generous employment of "606" in hundreds of patients using thousands of injections. We have seen a few patients with severe headache after treatment but encountered paresis of the eye muscles in only three or four cases. These favorable results may be due to the fact that we administer energetically repeated doses right from the beginning and seldom confine ourselves to one single injection. In new cases we usually combine "606" with mercury treatments, holding to the principle of repeated treatment. It is quite possible that, in this way, we may have prevented or quickly overcome the localizations of spirochetes in nerves, canals of the bones and so on.

In view of the great success which has attended the treatment with "606," attention must be paid to its harmful effects as well as to fatalities, although these are exceedingly rare and occur only under peculiar circumstances, usually inaccessible to investigation. We must criticize mercury and any other good remedy in the same manner. It is clear to everyone that by doing this we take upon ourselves a heavy burden of conscience and responsibility. But without energetic action a real treatment of syphilis is simply not possible.

Furthermore we must think not only of the individual who might be harmed but of the advantages that actually thousands, and tens of thousands of persons and therefore humanity, will gain through Ehrlich's method. Shall we, just because of rarely occurring disturbances dreadful not only to the patient but also to the physician, withhold from humanity the improvements in the treatment of syphilis which we owe to the introduction of arsenic preparations? Certainly "*nil nocere*" should be the guiding rule of the physician, but is harm done only by action? Is not the omission of something useful harmful also?

I have no doubt that we can achieve something helpful in every case which we treat with "606," although sometimes it may be uncertain which method should be applied. I cannot give any special indications because I treat every syphilitic with "606" whenever possible.

What unprejudiced person with real experience and abundant material will deny today that "606" is an excellent remedy and that by using it we achieve much greater therapeutic success than formerly? Generally the enemies of a method are found not among those who apply it, but where it is not used. It may be admitted that the remedy fails here and there and that relapses do occur occasionally, but has the method of treatment been studied in every such negative case? What individual doses were administered? What total dosage was used? What method was applied? I believe it is safe to claim in most cases that where the remedy has failed it was not due to lack of intrinsic value but to wrong and improper application. Naturally the remedy cannot produce miracles. It cannot achieve everything in every case, but it accomplishes such fine results that we should be very happy to have it. Indeed, are all the strange and novel sensations experienced during the treatment of a patient with "606" really unfavorable? I recall, for instance, those often-described isolated early relapses that look so much like tertiary processes. They seem to prove only that syphilis treated with "606" passes much more rapidly into a tertiary "phase," that much more quickly the generalized condition with its disseminated eruptions changes to a less dangerous, more localized one, and that we move much more quickly toward the termination of the disease than we did before.

When, formerly, has one seen so many patients cured during the early months of illness as now with these syphilitics who not only remain many months without symptoms but who repeatedly react negatively? When has one seen so many old syphilitics (without symptoms but showing positive reactions) who complain of all kinds of more or less objectively demonstrable symptoms, but who after a treatment start to "bloom again," showing joy of life and become healthy people as though newborn?

I know that many will laugh at my enthusiasm, but I maintain a very sober and skeptical examination of my abundant material, especially my repeatedly and continually observed private patients. I know that these improvements are not imaginary successes achieved through suggestion but that there is true eradication of formerly-existing, though not clearly-defined, pathological processes.

To me salvarsan is not simply a remedy for certain particular cases of lues. It is my very strong conviction that we are obliged to make the advantages of it available to every syphilitic in every stage of development. I consider the following conditions as contra-indications: extreme cachexia, severe advanced tabes, general paralysis, all cases of suspected

degeneration of the myocardium and alcoholism with all its more or less evident sequelae, particularly the damage to the blood vessels. In all such cases the physician, in his own interest, will do very well to administer small doses and to secure the patient's explicit consent if he intends to give intravenous salvarsan treatment. This is necessary in any case in older people.

In regard to *tabes*, I want to mention that I have seen such splendid and lasting results that here too I try salvarsan in nearly all cases. Before starting I naturally explain to the patient that he may not count with certainty on successful treatment, that there cannot be replacement of already damaged tissues and that one can only hope for an influence on the "irritation phenomena." With these reservations I advise the treatment.

Much more unfavorable are the conditions pertaining to paresis. The more I see, the more I am under the impression that the paralytic process is hastened by "606." This may show in severe attacks or in the very provocation of a dormant paralysis. Of course the situation is often rendered more difficult by the fact that it is not always possible to make an absolutely reliable differential diagnosis between a genuine paresis and a purely luetic "pseudo-paralytic" affection of the brain. From a practical point of view one may say, therefore, that trial with "606" is justified in every case of suspected general paralysis of the insane. In the event of a real paralysis the battle is lost anyway, and if it is "pseudo paralysis," "606" may help generally and perhaps even cure.[6]

In discussing the mode of employment of salvarsan it seems useless to me to recapitulate all the changes reported in the past year. The conclusions are very simple. Subcutaneous and intramuscular injections cause induration with marked permanent effects and very acute though comparatively unimportant immediate reactions. In intravenous injections the acute reaction is predominant while the after-effect remains obscured in the background.

In my opinion and experience the intravenous injection is the best and most important method. In most cases it is very convenient, easy and administered with the simplest apparatus imaginable; a rubber tube and a needle. It is possible to give it without hospitalizing the patient for more than a day, if at all, and if one masters the technique of needle insertion there are no disturbing after affects such as infiltration, necroses and so on.

[6] See my Diskussions-Bemerkungen, *Berlin klin. Wchnschr.*, 1911, No. 3.

Indeed, when looking over the innumerable inventions of new apparatus for intravenous injections I can scarcely restrain a smile. We make perfect infusions with the instruments we have used from the start, a slender glass irrigation flask filled with sodium chloride solution, a rubber tube and a needle. The only trick is the use of a glass tube inserted in the rubber hose about 8 to 10 cm. from the needle. After piercing the vein one can observe at once the blood flowing through this little glass tube providing proof that the needle hit the vein. After removing the tourniquet, and with the needle placed correctly, the sodium chloride solution flows along the glass tube and into the vein, flushing through the blood. Only when this is seen is the "606" solution poured into the flask. Subsequent rinsing is unnecessary if the needle is removed from the vein in one short pull.

On the other hand, in all intramuscular injections the tissues become necrosed to a greater or less degree. I prefer either the "Joha" ointment of Schindler or suspensions in oleum sesami because a relatively large amount of "606" can thus be incorporated in a very small total quantity.

The Schindler ointment is a stable, sterile, 40% "606" oil, having salvarsan distributed in an emulsion like a thin salve and is made up with Jodipin and pure sterile anhydrous lanolin. This mixture stiffens at ordinary room temperatures. For use the little ampule containing the oil is held in hot water until the mixture is a thin liquid which can be sucked up by a thin canula. According to the usual practice in my hospital the point of injection is located in the outer third of the so-called Duhot line which runs from the anterior spine of the ileum to the point of the sacrum. In order to be sure not to hit the nerves one injects somewhat obliquely outwards until one hits the fascia in the extreme outer third, just as in the case of mercury injections. The skin is sterilized with iodine. After inserting the canula one must make sure, just as in the case of mercury injections, that no blood vessel is punctured. One must never use for the injection the same canula which was used to suck up the preparation because of the danger of erosion in the canal of the needle. The patient must refrain from moving around for several hours after the injection in order to avoid possible leakage of the injected salvarsan.

The salve is manufactured as a 40% Dioxydiamidoarsenobenzol oil under the name "Joha" by Dr. Kades' Oranien Pharmacy (address Berlin S. O. 25 Oranienplatz). There also are available accurately graduated hypodermic syringes. The ampules ready for use contain 1.0 (equal to 0.4

salvarsan) or 0.5 (equal to 0.6 salvarsan) of the 40% oil mentioned above.[7]

Heinrich and Tatarsky[8] have devised a very practical syringe which offers the advantage that any physician is able, at will, to prepare a perfect suspension in the same syringe which he uses for the injection. Thus he has the guaranty that the amount of salvarsan to be injected is suspended in a very small amount of oil. (The syringe is supplied by Georg Haerkel, Breslau, Albrechtstrasse, 42). I confess that because of local necroses I use intramuscular injections very seldom. I am trying to get the lasting results expected of intramuscular injections by using repeated intravenous injections of "606" since these intravenous infusions also are cumulative.

We have seen no lasting harmful effects due to repeated intravenous injections, though we have given five and six injections to many patients. Disturbances occurring on the day of injection such as vomiting, diarrhea, chill and temperature cease, with a very few exceptions, by nightfall. Dizziness, loss of appetite and flatulence may persist for a little while afterwards. Occasionally a case appears which shows scarlatinoid and petechia-like eruptions of the skin. Infrequently one sees a similar eruption of the pharyngeal membrane accompanied by high temperature and deep exhaustion. Sometimes there is heart involvement lasting four or five days. Once we saw an acute yellow atrophy of the liver which was possibly an effect of salvarsan. I am sure it will be possible to reduce the incidence of these symptoms if we prolong the intervals between injections and thus reduce the accumulation.

The combination of the infused solution (0.6% NaCl solution, absolutely sterile and alkaline[9]) with salvarsan seems to play an important part. Different brands of salvarsan do not seem to be exactly alike. One must also take into consideration idiocyncrasies of the patient or of individual organs, particularly where the arsenic separates from the whole chemical complex.

[7] Carl Schindler: Über ein 40 proz. Dioxydiamidoarsenobenzolöl. *Berlin klin. Wchnschr.* 1910, Nr. 52.

[8] Eine neu Injektionsspritze für die intramuskuläre Salvarsanbehandlung. *Deutsche med. Wchnschr.* 1911. Nr. 14.

[9] Our procedure is as follows:

1. Dissolve the drug in warm 6% NaCl solution (about 5 to 10 cc.)
2. Add 200 to 240 cc. 0.6% NaCl solution (according to the dose.)
3. Alkalize with 4% NaOH until the sediment is completely dissolved. In this way very little alkali is necessary.

We have not sufficiently tried the acid solutions recommended by Duhot (0.4 to 0.6 to 300 cc. physiological NaCl solution).

As a curiosity I want to mention here the statements of a number of patients who say that during an injection they notice itching and burning of the gums (usually in cases of mild stomatitis) and claim to experience the odor of ether.

We have never observed the formation of massive thromboses in the injected vein.

Observations point to the fact that some patients naturally have or acquire a kind of hypersensitivity. Belonging to this category I count a few observed to have vasodilator erythema which appeared suddenly during the injection with acute and circumscribed swellings of the skin and mucous membranes. These can be interpreted only as "acute edema" similar to urticaria.

Other patients, having experienced a particularly violent reaction together with fever and exanthema, often show similar phenomena marked by a sudden appearance of rather alarming symptoms at each repeated injection.

Our methods for the use of "606" are as follows:

Two successive intravenous injections of 0.3 to 0.4 to 0.6 per dose at intervals of from three to eight days depending upon the age and constitution of the patient.

Either an intramuscular injection of 0.4 to 0.6 five to eight days after the second intravenous injection *or* a third intravenous injection following the second one by three to four weeks.

Instead of administering an insoluble suspension of "606" I usually give, in intervals of one week, two or more injections of Arsenophenylglycine, each in 0.5 cc. aqua distillata with an addition of 0.05 novocaine. These injections are almost always painless. They never cause an infiltration and when given once a week seldom cause unpleasant phenomena.

Arsenophenylglycine [10] (like Arsenobenzol, a trivalent-arsenic preparation recommended earlier by Ehrlich as preparation "418" for trypanosome affections) may not act quite as powerfully on spirochetes as does "606," but nevertheless is very useful for many purposes in the treatment of lues.

As may be seen I am a devoted and convinced supporter of the new remedy for syphilis. Whether or not it is superior to mercury, in many *ways it is in any event an antitoxin against the syphilis spirochete but it is an antitoxin which attacks the virus differently from mercury. Obviously*

[10] *Vide* Neisser. *Beiträge zur Pathologie und Therapie der Syphilis.* Berlin, 1911, p. 271 and following.

the ultimate result must be better if the enemy is attacked from two sides than from one only. Therefore, in spite of enthusiasm for "606" I seldom omit mercury treatments. It seems to me that more striking and, most important of all, more lasting results can be achieved by combining both remedies than by using each one separately.

I believe that in the near future we will make great progress in combined therapy. Judging from my own experience I may say that the antimony preparations first tried out by Salmon will also soon play an important therapeutic role in combinations with mercury and arsenic.

It must be stressed most vigorously, in view of its hitherto careless use in daily practice, that mercury treatment can be considered valuable only by using a known brand and a sufficient amount of mercury. However, it is important which mercury preparation is injected.

The following should be considered before choosing a mercury preparation:

1: Its mercury content which, as the following list shows, varies a great deal and explains easily the variety of effects and phenomena.

Name of preparation		% of Hg.	Individual doses	Hg. content
Mercuric benzoic oxide	1%	43.5	1 cc.	0.00435
Mercuric cyanate cryst.	1%	79.36	1 cc.	0.007936
Mercuric oxycyanate	1%	85.47	1 cc.	0.008547
Mercuric chloride	1%	74.0	1 cc.	0.0074
Mercuric chloride		74.0	2 cc.	0.0148
Mercuric chloride		74.0	5 cc.	0.0370
Mercuric salicylate	10%	59.0	1 cc.	0.059
Mercuric Thymol	10%	57.0	1 cc.	0.057
Calomel	10%	85.0	1 cc.	0.085
Asurol	5%	40.0	1 cc.	0.02
Asurol		40.0	2 cc.	0.04
Asurol		40.0	3 cc.	0.06

Calculating the above mentioned amount of mercury for a 6 weeks cure I inject:

1. For 42 injections: 1 cc. each of 1% sublimate solution — 0.42 sublimate — 0.31 mercury.
2. For 15 injections: 2 cc. each of a 5% asurol solution — 1.5 asurol — 0.61 mercury.
3. For 15 injections; 3 cc. each of a 5% asurol solution — 2.25 asurol — 0.94 mercury.

4. For 11 injections; 1 cc. each of a 10% mercuric salicylate suspension — 1.1 mercuric salicylate — 0.65 mercury.
5. For 11 injections; 1 cc. each of a 10% calomel suspension — 1.1 calomel — 0.94 mercury.
6. For 5 injections; ¼ cc. each of oleum cinereum — 0.70 mercury.

2: The rapidity of the absorption and the rate of elimination of the mercury.

> It must be emphasized that not only all soluble mercury salts, but also the much-used salicylate of mercury are absorbed and eliminated very rapidly. Elimination of oleum cinereum is somewhat slower and in using the preparation, caution is advised that cumulation may be prevented.

So far I have spoken only of treatment by injection. Indeed, I am convinced that the method is so superior to all others, inunction as well as oral administration, that practitioners should use no other.

Inunction is really important only for the treatment of skin exanthema where it acts as a local agent on widely disseminated spirochete nests. Except for this advantage treatment by inunction is inferior to treatment by injection, not to mention its inconvenience and frequent impracticability, since it is impossible to judge even approximately the amount of mercury actually absorbed by the body. Also, the inclusion of important hydrotherapeutic measures is certainly less reasonable with inunctions than injections.

It is possible, by the use of oral administration, according to the number of doses, to achieve the most effective results, particularly with calomel. But these good results are gained at the cost of very inconvenient secondary effects, such as enteritis and stomatitis.

The principle of our combined treatment is as follows: On one hand we want a rapid attack which will destroy the spirochetes as rapidly as possible. At the same time we wish to secure a lasting check to further development. Therefore, we combine intravenous "606" injections with mercurial preparations which can be absorbed rapidly (especially asurol) and remanent preparations (especially oleum cinereum).

An excellent "grey oil" (ol. cinereum) is manufactured at my request by the Engel Pharmacy (Breslau IX, Scheitniger Strasse 28). It corresponds to the new French preparation. I have used it for a long time and can recommend it, for it agrees much better with the patient than many

other insoluble mercury preparations and yet permits a full dosage of the mercury. The effect is not a very rapid one and therefore it is adequate only for persons without dangerous symptoms which demand prompt removal.

The oil contains forty percent metallic mercury. Certain syringes, manufactured especially for this purpose, are needed for the injection. The one made by Barthelemy holds ¼ cc. oil, equaling 0.14 mercury, and has 14 graduations so that each division represents 10 mg. of mercury. The one manufactured by Zieler, the Record Syringe, is divided into fifteen graduations and contains ⅜ cc. so that ten divisions correspond to 0.14 mercury.

It is not necessary to sterilize the syringe and needle each time they are used if they are always kept in liquid paraffin.

The needle is filled with pure liquid paraffin and then fitted to the syringe filled with grey oil. The injections are usually made deep into the glutei. In order to prevent the formation of emboli the syringe should be removed from the needle after the flesh is pierced to ascertain whether blood is coming from the needle. When withdrawing the needle one should make sure that the skin immediately surrounding it is deeply pressed down in order to avoid having the oil flow back into the track of the needle.

For initial injection I use, in most cases, half a Barthelemy syringe or 5 graduations of a Zeiler syringe which is the equivalent of 7 centigrams of mercury. If there are no contraindications such as weak constitution, low weight or an extreme sensitivity at the site of injection, the full contents of a syringe may be administered at each subsequent injection. When using half the contents of a syringe I give two injections per week. When using the full contents I give one each week only.

A full course of treatments consists of ten full injections or twenty half ones. I give the injections in two periods with a pause of at least five to six weeks after the first five whole or ten half injections. Only then, after making sure that there are no secondary effects from the mercury do I administer the second portion. The interval is necessary in order to make sure that there are no sudden developments of stomatitis or enteritis originating from the accumulation of mercury, because when using grey oil one must always expect vigorous after-effects which last for weeks.

In every case a careful check of the urine is necessary. There must be very strict care of the mouth. Repeated cleansing with an isoform tooth-paste and frequent gargling are essential.

To avoid unexpected and disturbing sequelae grey oil should not be

used in cases in which there is disease of the internal organs (kidney, intestines or liver) or when there is a chronic intoxication (alcohol, lead, tobacco). It should not be administered to old people or be given to cachectic, goiterous, arteriosclerotic or tubercular patients, nor to pregnant women with kidney damage.

The danger of injection with grey oil is that sometimes the mercury of some of the individual injections may not be well absorbed. If this absorption does not take place one has, at the end of the cure, a great number of deposits containing considerable mercury. If then, later on, absorption from all these deposits takes place at once, the enormous quantity of mercury suddenly freed in the body may lead to a dangerous, even a fatal, condition. For the same reason one should never make an injection twice into the same place. By tenderness on palpation and by the spontaneous sensation of pain on the part of the patient we make sure that we do not use again a former place of injection. Whenever hard solid infiltrations develop regularly after injection, and these vary greatly from one individual to another, one should either stop the treatment completely or use only half a portion each time, administering the dose at greater intervals.

Asurol (a double salt of mercuric salicylate and amido-oxybutynate of sodium with a content of 40.3 percent mercury) has the advantage that it is easily soluble and does not precipitate albumen. Therefore, it is a quickly absorbable salt. With corresponding rapidity its mercury is eliminated. This explains the fact that asurol displays a very energetic and lasting effect. Usually we inject 0.1 asurol, which is equivalent to 0.04 mercury, per dose, two or three times a week. We combat its frequently painful effects by using, in a 2 cc. syringe, the following solutions in order:

1. 1 cc. of a 10% asurol solution
2. 1 cc. of a 2% novocaine solution

Such mixtures are not stable and therefore the method just mentioned is very practical. Recently we have studied related salts which are indicated as Asurol New B (a double combination of sodium oxymercurisalicylic acid and diaethylbarbituric acid with 35.7 percent mercury content), and Asurol New C (a double combination of sodium oxymercurisalicylic acid and sodium barbituric acid with a 39.6 percent mercury content). It is best to use these salts in solutions as fresh as possible. A dye manufacturer (formerly Frederick Bayer in Eberfeld), now supplies Asurol New C dissolved in distilled water in 20 cc. ampules so that one has a

solution in which 2 cc. contains 0.04 mercury [11] the dose for injection. The new salts will not combine with novocaine. The procedure is as follows:

1. 1st day; intravenous 606, 0.3 to 0.4 to 0.6%.
2. 4th day; asurol; 2 cc. of a 5% solution equivalent to 0.04% mercury.
3. 8th day; intravenous 606, 0.3 to 0.4 to 0.6%.
4. 11th day; asurol equivalent to 0.4% mercury.

   One to four may follow each other more closely so that the four injections can be given within eight days.
5. 14th day; asurol equivalent to 0.04% mercury.
6. 18th day; oleum cinereum equivalent to 0.07% mercury.
7. 21st day; oleum cinereum equivalent to 0.07% mercury.
8. 25th day; oleum cinereum equivalent to 0.07% mercury.
9. 29th day; intravenous 606, 0.3 to 0.4 to 0.6%.
10. 32nd day; oleum cinereum equivalent to 0.14% mercury.
11. 39th day; oleum cinereum equivalent to 0.14% mercury.
12. 46th day; oleum cinereum equivalent to 0.14% mercury.

Naturally there can be modifications. For instance, one may use only oleum cinereum in the first week or, instead of asurol, one may use other soluble and insoluble preparations which must be chosen with the same two-fold aim.

In spite of my conviction of the healing power of salvarsan I have not deserted the principle of long-continued treatment. Through my efforts the theory first laid down by Fournier, that syphilis is a chronic disease and must be treated essentially by long-continued intermittent course of treatment is now accepted in Germany.

The principle of persistent treatment was given *eo ipso* by the experience that in most cases it was not possible to eradicate syphilis with a single treatment. Too often early clinical relapses and later recidives showed that if treatment were insufficient in the beginning, clear cut lesions appeared even after years and decades of apparent cure. So one gradually accepted the rather pessimistic principle never to trust a patient but always to consider the possibility of a relapse. Accordingly in every case we give several courses of treatment throughout three or four years, whether or not there are any symptoms. As far as one can prove anything at all by statistics this principle has been justified. In fact, it seems that the cases with continued treatment do better and escape relapses of a tertiary nature more often than those treated with mercury once only or not treated at all.

[11] A. Neisser: Asurol, ein neues Quecksilbersalz zur Syphilis-behandlung. *Therapeutische Monatshefte*, Dec. 1909.

The principle of alternating treatments is based on the idea that the body or the poison develops a tolerance to the medication and that as a result, the medicine loses its efficacy. I also suggest rotation between a very energetic treatment and a milder one in cases in which absence of a relapse indicates a lighter development of the disease.

The justification for treatment during symptom-free periods was long disputed. Now from experiments with animals we know definitely that such specific remedies as mercury and arsenic preparations and perhaps also iodine preparations and quinine not only eliminate pathologic anatomic products of syphilis, but destroy the very spirochetes not only in active foci of affection, but also those in a state of clinical and pathologic-anatomic latency. Therefore we have the right, even the duty, to begin treatment not only when there are clinical symptoms but whenever we have reason to believe that syphilis still is in the body. This is the case wherever there is a positive serodiagnostic reaction.

It is just these serodiagnostic experiences which show us how often internal well-being and the absence of symptoms occur with still-existing latent syphilis. Day by day we ourselves, who have demanded a very intensive treatment for more than thirty years, see how we have underestimated the difficulty of achieving cure. It is my conviction that hitherto the majority of lues cases have remained uncured. This explains the enormous number of delayed heart and aorta lesions as well as the tabes, paresis and tertiary organic diseases of all kinds. On the other hand it explains why the number of reinfections is minimal.

Thus we cannot dispense so easily with the chronic treatment. Perhaps it will not be necessary any longer to carry it through as schematically as before. Perhaps it will not be necessary to submit each case, without exception, to a treatment of three or four years, as we demanded formerly. Perhaps by frequent serodiagnostic checking we shall be able to divide the syphilitics into two groups, the first who show repeated relapses or positive reactions for a long time and therefore need continued treatment, and the second group who show a negative reaction relatively soon and reproduce this reaction at repeated examinations. Those of this last mentioned group perhaps could be dismissed from further treatments. However, it must be pointed out explicitly that as yet we are not sufficiently informed concerning how long a man can produce a "negative reaction" yet carry in his system syphilis which may later show as a relapse or a positive reaction. Unfortunately, because of this doubt, we cannot for the time being, draw such a dividing line between two kinds

of syphilis. As a general rule, now as before, we have to keep to the principle of long-continued treatment, although the time under therapy may be shortened to one and a half years. In many cases it might be superfluous to continue treatment of patients who had reacted negatively two or three times but the danger of losing ground already gained, through temporary interruption, is too great and continued treatment should therefore always be considered as a matter of caution.

Even if the reaction remains negative on repeated examination I make it a rule to repeat treatment. The more recent the infection, the more important is the repetition of the treatment. I am never satisfied with one course only. Experience has taught that even though as many as three negative reactions substantiate a single energetic course of treatment positive reactions and new symptoms of syphilis may later be seen. Had treatment been continued in such a case, in spite of negative reactions, a definite cure would have taken place.

Considering these experiences has the negative reaction diagnostic significance as a guide? I believe that it is thoroughly wrong when, in exaggerated objectivity one says: "the negative reaction is no proof." On the contrary, I believe that a negative reaction can be of the utmost value for practical purposes, provided that a very careful and absolutely trustworthy examination has been made, even though it does not remove all uncertainty at once in every case. We classify patients reacting negatively as follows: latent syphilitics (people with a definite syphilitic anemnesis yet without evident symptoms at the moment) and people with syphilis of which one knows nothing at all. Among the latent syphilitics one has to distinguish again between "early-latent" syphilitics (those with an infection of short duration) and the "late-latent." The older the syphilis is, the more one is justified in concluding, after observing a negative reaction, that it is not a latent period, but an accomplished cure.

In those patients of whose syphilis nothing is known at all, one must consider the anemnesis and all accompanying circumstances. However, after one single treatment the negative reaction provides reason to hope that the syphilis is absolutely cured or that it has never existed. The certainty increases if the result of repeated serodiagnostic examinations made at not too long intervals is a constantly unchanged negative picture. It would be wonderful indeed if, in the course of a few hours, one could dismiss every anxiety, doubt and uncertainty in regard to the question "syphilis or not syphilis." Unfortunately this is not yet possible but it is a great blessing that it is possible to obtain the confirmation at all. Where we have had to depend entirely on deductions, convictions and faith, we

are now able to obtain apparently correct information in the course of a few months. Therefore the negative reaction is of great importance. Only one must know how to value it within our total problem.

We must not forget another important factor which influences the reaction: the specific treatment with mercury and arsenic. It is established with certainty that a positive reaction can be changed into a negative one by energetic treatment with mercury or "606." This phenomenon can have two explanations:

1. The complement-binding substances of the serum can be directly destroyed by the introduction of the drug.
2. It is possible that the disappearance of these substances is due to the destruction or disablement of a great number of spirochetes in the body so that the regeneration of the reaction bodies, the so-called "antibodies," ceases.

I cannot go into further details on this important point. In our opinion the second possibility is justified. We regard the change to a negative reaction through treatment as the evidence of damage done to the lues virus itself. We see in the reappearance of the negative reaction, a valuable yardstick for the measurement of therapeutic success.

It would be absolutely wrong to see a proof that a cure has been accomplished in a negative reaction immediately following treatment, and to interrupt the course of treatment at this point. The negative reaction at this time indicates only that our treatment has been effective and sufficient but it does not prove that all the spirochetes in the body are destroyed and that therefore the illness has come to an end. This is evident from the unfortunately frequent observation that the reaction, having become negative after a course of treatment, becomes positive again, sooner or later, so that a relapse occurs. We must not be tempted, especially during the early phases of lues, to cease to alternate treatment. Only a negative reaction repeatedly observed at long intervals, independent of treatment gives us the right to speak of a real cure.

We still call our treatment "continued intermittent," but when we examine our methods more closely we must say that although we treat intermittently the influence is a permament one. The mercury injected with oleum cinereum and the quantities of "606" injected intravenously remain in the body for a long time and are eliminated slowly so that both the body and the spirochetes are kept permanently under the influence of the spirocheticide, even if new injections are given only every one or two months.

Particularly for the accomplishment of our purpose it is of great advantage that we do not have to rely solely on mercury but have now a second remedy at our disposal. All intensive mercury cures require interruptions because of stomatitis, enteritis, beginning nephritis and other indications of mercury damage which otherwise occur. Today we replace these formerly unavoidable intermissions with "606" treatments which act as rapid killing strokes whereas the effect of the mercury is a chronic one, retarding the development of the disease.

My modus procedendi is the following:

Five to six weeks after the above-mentioned first course of treatment an examination of the blood is made. If the reactions is positive I undertake a second cure like the first. Of course the treatment of the case is adjusted in accordance with information gained in the meantime. There may be changes in dosage and in the intervals allowed between injections.

If the reaction is negative I give at least one more treatment of "606" intravenously. After five or six weeks more the blood is examined again and no matter what the result, "606" is given once more. Perhaps oleum cinereum 0.07 to 0.14% is given once weekly again until 0.70% of mercury is reached.

Eight weeks after the end of this treatment the blood is re-examined. If the reaction is negative this time we must make a serious decision. Can the cure be relied upon and the treatment stopped? Should one continue with some therapeutics from time to time? The negative reaction does not wholly prove that the cure is certain since the patient is constantly under the influence of therapeutic measures.

Only the experience of the coming decade will decide the matter. Until then it will depend upon the temperament of the physician and the patient whether, according to a pessimistic or optimistic attitude and to other attending circumstances, the physician will go on for a long time with the "continuing treatment" or will stop sooner, hoping that the many negative reactions and lack of symptoms may mean a complete eradication of lues.

I see no reason to treat patients who come to us in the late stages or in advanced years any differently than those with a new infection if the manifest symptoms or positive reactions demand treatment unless the general condition requires a special therapeutic regime. At most one should proceed with salvarsan and mercury even more vigorously and more consistently than ever, perhaps adding full dosage of iodine and hydrotherapy. Experience has taught us that it is much more difficult to

influence the reaction in chronic cases, that is to influence the spirochetes therapeutically, than in early stages of the disease following close upon infection.

Perhaps if all physicians will cooperate by making use of modern therapy we may live to see the time when the majority of lues cases no longer develop into latent forms of late stages but will be cured in the earliest incipient stages of the disease.

What we do for the individual patient, be it to cure him more quickly from the disease or to insure him a milder course, naturally serves the benefit of the whole population in the universal fight against syphilis as a contagious disease and a social calamity. The earlier and more quickly the individual patient can be rendered free of contagion the fewer sources of infection there will be. Thus the number of syphilitics will decline and there will be fewer of those thousands who, today, are doomed to an early death by the sequelae of the disease.

Human indolence and stupidity will arrange that syphilis will never die out but will remain always a dangerous disease, but we know that new and wonderful weapons have been placed in our hands to combat it. Let us practical physicians express our admiration and gratitude to those men who created the scientific foundations for these therapeutic triumphs: Schaudinn, Hoffmann, Metchnikoff, Roux, Wassermann, Bruck and Paul Ehrlich.

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NOTES AND COMMENTS

A DRAMATIC CLYSTER

B. J. WHITING

"The History of the Enema with some notes on Related Procedures" by Julius Friedenwald and Samuel Morrison[1] is so rich in details and fascinating in development that one hesitates to supply even a slight addendum. Nevertheless the relative scarcity of sixteenth-century material which the authors present, and especially the lack of English references before Shakespeare,[2] would seem to justify an account of the epic clystering described in John Heywood's *The Playe Called the Foure PP.* Heywood's play is first known in a print of 1545 or thereabouts,[3] but it had doubtless been composed a good score of years before that date. The play is a familiar document in the history of the English drama, and its plot, if its loose structure can be dignified by that term, is fairly well known. The Palmer enters and boasts of the shrines which he has visited and of the spiritual merit which he has won. As he is talking, the Pardoner comes on and asserts that his relics and pardons are a much easier and safer way to save souls. Before he has convinced the Palmer, the Potycary joins them and claims that he alone is the true soul-saver, since it is by virtue of his medicines that people get their start toward heaven. Hanging is an exception:

> That way perchaunce ye shall nat myster
> To go to heuen without a glyster.[4]

Now the fourth P, the Pedler, walks on and, after enumerating and exhibiting his wares, to the accompaniment of some rather bawdy talk from the Potycary, joins the others in a song. It is then suggested that he decide which of the three is the best soul-saver; he declines so responsible a duty, but readily agrees to judge which can tell the best lie. The others accept him as referee and then the Pardoner exhibits his relics, palpable fakes all, and the Potycary shows off his death-dealing remedies.

[1] *Bulletin of the History of Medicine*, VIII, 1940, 68-114, 239-276.

[2] P. 81.

[3] Reproduced in Tudor Facsimile Texts, London, 1908; a convenient modern edition is in Joseph Quincy Adams. *Chief Pre-Shakespearean Dramas*, Boston, 1924, pp. 367 ff.

[4] Sig. A iv; Adams, p. 369, ll. 175-6.

This serves as a sort of prologue to the contest and the Potycary proceeds to tell his lie, which contains the first and perhaps the most exaggerated account of a clyster in operation to be found in English literature:

If ye be set in merualynge
Then shall ye here a meruaylouse thynge
And though in dede all be nat true
Yet suer the most parte shall be new
I dyd a cure no lenger a go
But Anno domini millesimo
On a woman yonge and so fayre
That neuer haue I sene a gayre
God saue all women from that lyknes
This wanton had the fallen syknes
Whiche by dissent came lynyally
For her mother had it naturally
Wherefore this woman to recure
It was more harde ye may be sure
But though I boste my crafte is suche
That in suche thynges I can do muche
How ofte she fell were muche to reporte
But her hed so gydy and her helys so shorte
That with the twynklynge of an eye
Downe wolde she falle euyn by and by
But or she wolde aryse agayne
I shewed muche practyse muche to my payne
For the tallest man within this towne
Shulde nat with ease haue broken her sowne
All though for lyfe I dyd nat doute her
Yet dyd I take more payne about her
Then I wolde take with my owne syster
Syr at the last I gaue her a glyster
I thrust a thampyon in her tewell
And bad her kepe it for a iewell
But I knewe it so heuy to cary
That I was sure it wolde nat tary
For where gonpouder is ones fyerd
The tampyon wyll no lenger be hyerd
Whiche was well sene in tyme of thys chaunce
For when I had charged this ordynaunce
Sodeynly as it had thonderd
Euen as a clap losed her bumberd
Now marke for here begynneth the reuell
This tampion flew .x. longe myle leuell
To a fayre castell of lyme and stone
For strength I knowe nat suche a one

Whiche stode vpon an hyll full hye
At fote whereof a ryuer ranne bye
So depe tyll chaunce had it forbyden
Well myght the regent there haue ryden
But when this tampyon on thys castell lyght
It put the castels so farre to flyght
That downe they came eche vpon other
No stone lefte standynge by goddes mother
But rolled downe so faste the hyll
In such a nomber and so dyd fyll
From botom to bryme from shore to shore
Thys forsayd ryuer so depe before
That who lyste nowe to walke thereto
May wade it ouer and wet no shoo
So was thys castell layd wyde open
That euery man myght se the token
But in a good houre maye these wordes be spoken
After the tampyon on the walles was wroken
And pece by pece in peces broken
And she delyuered with suche violens
Of all her inconueniens
I left her in good helth and luste
And so she doth contynew I truste.[8]

After so valiant an effort it is a matter for regret to be forced to record that the Potycary did not win the contest.

[8] Sigs. C iv^{v}-D i^{v}; Adams, pp. 377 f., ll. 704-768.

MEDICO-HISTORICAL NEWS AND ACTIVITIES

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE

CONSTITUENT SOCIETIES

The Johns Hopkins Medical History Club, Baltimore, Md.

The Johns Hopkins Medical History Club opened its 55th year of activity with a meeting on November 27, 1944 commemorating the One-Hundredth Anniversary of the American Psychiatric Association. The meeting was held in the Lecture Hall of the Institute of the History of Medicine, with Dr. Adolf Meyer, Professor Emeritus of Psychiatry of the Johns Hopkins University, as Chairman. The two papers read were as follows:

Major Therapeutic Trends in American Psychiatry.
Dr. JOHN C. WHITEHORN

Origin and Growth of Child Psychiatry. Dr. LEO KANNER

An exhibit illustrating the history of American psychiatry was prepared for the occasion in the Exhibition Hall of the Institute. The pictorial material of the exhibit had been displayed at the Centennial Meeting of the American Psychiatric Association in May 1944 and was loaned to the Institute of the History of Medicine through the courtesy of the Association.

The New York Society for Medical History

On December 7, 1944 the Society held a meeting at the Squibb Auditorium, 745 Fifth Avenue, New York City, to hear Professor Richard H. Shryock, Professor of History at the University of Pennsylvania, speak on "Factors Which Have Conditioned Medical Research in the United States."

NATIONAL NEWS

Horace Wells Centenary

The year 1944 marks the 100th anniversary of nitrous oxide anesthesia which was introduced by Horace Wells, a dentist of Hartford, Conn. On December 11, 1844, Dr. Wells submitted to the first operation performed under this type of anesthesia.

A number of events throughout the country have marked the centenary. On September 21, 1944, a resolution commemorating the event was passed by the United States Senate. A special meeting of the Connecticut State Medical Society and the American Dental Association was held in Hartford on December 11, 1944, to pay tribute to Wells and to unveil a plaque marking the site of the dentist's former home. The speakers included the following: Dr. Howard R. Raper, Dr.

Theodor Blum, Dr. Emery A. Rovenstine, Dr. Charles J. Wells, Dr. Arno B. Luckhardt, Gov. Raymond E. Baldwin, Senator Francis Maloney, Dr. H. Gildersleeve Jarvis, Dr. Walter H. Scherer, Dr. Arthur H. Merritt, and Dr. Thomas Parran. The November issue of the *Connecticut State Medical Journal* was named the Horace Wells Centenary Number.

The District of Columbia Medical Society celebrated the event by unveiling a bust of Wells in the Medical Society Auditorium. In San Francisco a two-day meeting was held on December 10 and 11 during which a tree was planted and a memorial tablet dedicated in Golden Gate Park. The formal exercises at the College of Physicians and Surgeons included addresses by Dr. Chauncey D. Leake and Dr. William B. Neff.

In Baltimore the Enoch Pratt Free Library prepared a very interesting window display to bring the event to the attention of the people of that city.

Illinois

The Second Annual D. J. Davis Lecture on Medical History was held on November 13, 1944, at the University of Illinois College of Medicine. Dr. Henry B. Ward, Professor of Zoology, Emeritus, University of Illinois spoke on "Medical Zoology in America's First Century" to an audience of 200 faculty members and students. Dr. Ward's long and distinguished career includes important contributions to both biology and medicine.

The D. J. Davis Lectureship was established by associates and friends of Dr. Davis, now Dean Emeritus of the College of Medicine, University of Illinois, upon his retirement in 1943. During his thirty years at the University of Illinois in addition to his outstanding work in bacteriology, public health, and medical education, Dr. Davis maintained an active interest in medical history and promoted research in the field. The Lectureship was established in order to pay tribute to him and to provide a means whereby his interest in medical history would be perpetuated and others stimulated. The Inaugural Lecture in 1943, "A Prelude to Medical History," was delivered by Dr. J. Christian Bay, Librarian of The John Crerar Library, Chicago.

David Hosack

Mrs. Claire K. Feins (61 East 182nd Street, Bronx, N. Y. 53) is seeking letters, pamphlets, and other materials relating to the life of Dr. David Hosack (1769-1835) of New York. Dr. Hosack was professor of medicine at Columbia College, College of Physicians and Surgeons, and Rutgers Medical College in New York; he edited scientific publications, carried on a voluminous correspondence (especially on the contagious nature of yellow fever), wrote memoirs of DeWitt Clinton, Benjamin Rush, Caspar Wistar, etc. etc. and was active in the development of societies of medical, historical, botanical, artistic, and useful nature in New York. His letters are likely to be included in the papers of contemporaries longer remembered than himself, and Mrs. Feins will be most grateful for any information that will help her to round out this doctoral dissertation at Columbia University.

NEWS FROM LATIN AMERICA

Argentina

The most recent issue of *Revista Argentina de Historia de la Medicina*, Vol. III, No. III, September 1944, which appears regularly under the editorship of Prof. Dr. Juan Ramon Beltran, contains the following original articles:

Antolín Bedoya Villacorta: La medicina en el imperio de los Incas
Juan Ramon Beltran: Rosas y el Instituto Jenneriano
Luis Dellepiane: Los conocimientos anatómicos de Ambrosio Paré
Félix Martí Ibáñez: Preludio a la historia de la sífilis

NEWS FROM EUROPE

England

We have received news of the death of Dr. Thomas Hancock Arnold Chaplin in London on October 18, 1944, aged 80. Dr. Chaplin was well known to most medical historians as the former President of the Section for History of Medicine of the Royal Society of Medicine and the author of "Medicine in England During the Reign of George III," "A St. Helena Who's Who," as well as two works on the illness of Napoleon.

Turkey

An issue of *Türk Tib Tarihi Arkivi* (Archives of the History of Turkish Medicine) which has just been received shows that studies in medical history are still being carried on vigorously in Turkey. The center of such activities is the Institute of the History of Medicine at Istanbul University, under the leadership of Dr. A. Süheyl Ünver.

BOOK REVIEWS

GEORGE ROSEN, M. D. *The History of Miner's Diseases. A Medical and Social Interpretation.* With an Introduction by Henry E. Sigerist, M. D. New York: Schuman's, 1943. xii + 490 pp., 20 ill. $8.50.

In a first part the author deals with miner's diseases from neolithic times to the end of the 18th century. The existing data on mining in the neolithic and antiquity, though socially extremely interesting, do not permit identification of definite diseases, except perhaps for hookworm. The same holds true for the Middle Ages. Only with the great Renaissance classics on miner's diseases, Agricola and Paracelsus (we possess fortunately excellent English translations of the former by Herbert C. and Lou H. Hoover, of the latter by Dr. Rosen himself) do we touch firmer ground. For the 17th and 18th centuries the author analyzes mainly the contributions of the followers of Paracelsus, as collected by Koelsch, and of the father of industrial medicine, Ramazzini. For the 19th century with the enormous development of industry and science the material swells to such proportions that the author has to limit his enquiry mainly to one branch of mining: coal mining, and to one disease: the so called "collier's lung." This analysis which forms the second part of Dr. Rosen's book, takes almost two-thirds of his space, although the author has already limited his subject, and although only part of the existing literature (as for instance a comparison with the Index of the Surgeon General's Library shows) is reviewed. In this second part Dr. Rosen gives—besides important chapters on the evolution of mining conditions, on morbidity and mortality of miners, on therapy and prophylaxis, on social and protective legislation—an extremely interesting, detailed study on the evolution of clinical and pathological knowledge of the "miner's lung" during the 19th century. He follows this evolution in the work of the Scotch clinicians of the 1830's, German pathologists and Belgian physicians in the 1860's, up to the relative solution of the problem in the work of Greenhow (1869) and the decrease of frequency and interest in the disease towards the end of the century. It is to be hoped that conditions will soon enable Dr. Rosen to realize his plan of a second volume which would not only deal with the important developments in our knowledge of pneumoconiosis during the first decades of the 20th century, but also give more detailed attention to miner's nystagmus, pulmonary neoplasms, and miner's anemia, scientific knowledge of which has been obtained mainly during the 20th century.

With this treatise on the history of miner's diseases Dr. Rosen has done pioneer work and struck an extremely rich, but so far sadly neglected, mine of medical history: the history of occupational diseases. It is not an exaggeration to say that with his close integration of data on technical, social, pathological and scientific evolution Dr. Rosen has most successfully created a new genre of medical historiography, and that his extremely readable and well illustrated book will be of great value not only to the historically minded physician or public health man, but beyond these limits to all those concerned with the evolution of society.

ERWIN H. ACKERKNECHT

BERGEN EVANS (in consultation with GEORGE J. MOHR, M. D.). *The Psychiatry of Robert Burton.* New York: Columbia University Press, 1944. ix + 129 pp. $2.00.

Robert Burton's *Anatomy of Melancholy* is probably known to every educated man, but has as likely been read by very few. Professor Evans points out that although dealing with a psychiatric subject, the book has received but scant attention as a psychiatric document. His own purpose is "to present Robert Burton's theories of psychiatry and to evaluate them in the light of modern psychological knowledge" (p. viii). This task being a psychiatric as well as a literary one, Professor Evans wrote the book in consultation with George J. Mohr, M. D. The result is a short but very stimulating volume dealing with Robert Burton himself, his work on melancholy, and the symptomatology, etiology and therapy of melancholia propounded by him.

Professor Evans and Dr. Mohr found that Burton's views on melancholy are surprisingly modern. The disease is of the body and the mind, yet preëminently a mental one, largely caused by heredity, unconscious urges and conflict with society, characterized by anxiety, aggressiveness, feeling of guilt, etc., and is best treated by what we may almost call an analytic approach in the modern sense. It is admitted that Burton's concept of melancholy includes mental conditions which today would be classified differently, that his views are tinged by the traditional concept of the humors and even by magic and astrological ideas, and that he does not altogether reject the treatment by purgatives favored by the physicians of his time. It is furthermore believed that Burton's own suffering from melancholy gave him the remarkable insight into the mental state of the neurotic patient and helped him to find his path through the labyrinth of ancient and contemporary literature which he not only perused but also constantly quoted.

There can be little doubt that the views as presented by the author are actually to be found in Burton's work. Yet this reviewer is not quite certain whether the presentation of a modern psychiatric picture has not been arrived at by a process of selection from a modern point of view. For a book that calls itself "*The* Psychiatry of Robert Burton," the large sections which lie in a direction different from the thread followed have not been given sufficient consideration.

The booklet is relatively little concerned with the traditional background against which Burton's work originated. It does not go into lengthy explanations of the humoral theory which formed the concept of melancholia (the disease caused by the black bile); nor does it analyze the many contemporary works on the same subject.[1] This concentration on Burton's work itself helps to drive the point home but is not without a serious drawback. Just where Burton is believed to be so very modern he is on the contrary very old fashioned. Professor Evans writes:

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[1] For a comparative survey of contemporary works on melancholy *cf.* Sanford V. Larkey's introduction to *A Discourse of the Preservation of the Sight: of Melancholike Diseases; of Rheumes, and of Old Age*, by M. Andreas Laurentius, translated by Richard Surphlet, 1599. Oxford University Press, 1938. [Shakespeare Association Facsimiles No. 15.]

"In his conception of the nature of the emotional basis of that distortion of the imagination which he felt to be the prime dynamic factor in neurosis he comes excitingly close to elaborating a theory of the unconscious mind. 'Perturbations and passions, which trouble the phantasy,' he says, in a passage which has already been quoted, but which is striking enough to be worth repeating, 'though they dwell between the confines of sense [feeling] and reason, yet they rather follow sense than reason, because they are drowned in corporeal organs of sense. They are commonly reduced into two inclinations, *irascible*, and *concupiscible*'" (pp. 103-104).

This is really the old Platonic doctrine of the tripartite soul, a doctrine which was accepted by Galen and which lived on into the seventeenth century. According to this doctrine, the concupiscible soul dwells in the liver, the irascible in the heart, and the rational in the brain. As long as this theory prevailed, conscious and rational processes were not considered the only psychic functions, nor was any gap seen between the body and the mind. There are passages in Plato and the later philosophers and physiologists which are as strikingly "modern" as any that can be found in Burton. As indicated by the author himself (p. 110 f.), the truth of the matter is that of late our own psychology is tending towards a view much closer to these old theories than was the nineteenth century. To some extent this accounts for our rediscovery of Burton's psychiatry and will probably help us to understand and appreciate other older psychiatrists who were neglected or derided not so very long ago.

These remarks should not be interpreted as an attempt at belittling Burton's merits—particularly since Professor Evans, in the Conclusion, warns of exaggerating his psychiatric achievements. Rather, they should help to emphasize the timeliness of Professor Evans' book and the attention it deserves.

O. Temkin

Cora Dubois, *The People of Alor. A Social-Psychological Study of an East Indian Island*. Minneapolis: The University of Minnesota Press, 1944. xvi + 654 pp., 8 ill. $7.50.

Dr. Dubois spent one and a half years in Atimelang, a complex of villages inhabited by about 600 people, situated on the Island of Alor in Netherlands East Indies, in order to study how this exotic culture forms a specific type of personality. For this purpose, Dr. Dubois has collected a series of eight autobiographies which fill about half of her book. She precedes these autobiographies with a synthetic study of the psychology and culture of the Alorese, derived mainly from the autobiographies. Though Dr. Dubois emphasizes that childhood experiences do not exclusively determine the mature character, the accent is on such childhood experiences. This has become rather customary with many American ethnographers since Freudian influences penetrated American anthropology and since Margaret Mead so successfully launched work along these lines 15 years ago. The original feature of Miss Dubois' book is that her results are compared with her own word association tests, and an analysis of Porteus Maze tests, Rorschach

tests, and children's drawings by analysts unfamiliar with her results. The latter confirm in many points Miss Dubois' observations. Furthermore the psychoanalyst, Dr. Kardiner, who was a spiritual and financial godfather to the enterprise, adds to the synthesis and each autobiography a comment of his own and diagrams of the different character structures.

Dr. Dubois' description reveals a society where men are involved in a complicated financial system of exchanges, similar to those described for other Melanesian cultures by Malinowski, Fortune, Faith, etc.; a system which has relatively little practical but enormous prestige implications. The actual providers are the women, entirely absorbed in garden work, and entirely void of status. The disruptive forces of this system manifest themselves in a very high divorce rate and countless financial quarrels. A loveless childhood, a youth full of frustrations are the inescapable consequences of this system which produces the peculiar Alorese character.

The medical field is only incidentally mentioned, as the author completely concentrated on her psychological problem and postponed publication of the numerous highly interesting ethnographical data not directly connected with her central theme. Nevertheless we learn such important facts as that illness often forces financiers into paying debts in order to placate supernaturals; that "possessed" (mentally diseased, probably also delirious) people are killed or even buried alive because they are regarded as dead; that there is no inclination towards trance, intoxication, and suicide, etc.

Dr. Dubois' important contribution will undoubtedly interest all those interested in the relations between anthropology and psychology.

ERWIN H. ACKERKNECHT

C. S. RAFINESQUE. *A Life of Travels*, being a verbatim and literatim reprint of the original and only edition (Philadelphia 1836). Foreword by E. D. Merrill. Critical Index by F. W. Pennell. Chronica Botanica, vol. 8, No. 2. Waltham, Mass.: the Chronica Botanica Co.; New York: G. E. Stechert and Co., 1944, 68 pp., 6 ill. $2.50.

Only during the last 60 years has it dawned upon Americans, that the strange man, who died poor and lonely in Philadelphia in 1840 after having lived for 27 years among them, was not the "inspired idiot" he had been thought of and treated accordingly, but one of the greatest glories of early American science, especially in the field of botany, zoology and anthropology. It seems he was even a great innovator in business, in inventing the "coupon" system in commercial papers. In his own case at least Rafinesque's hopeful statement, "But time renders justice to all at last" seems to come true.

This reprint of Rafinesque's autobiographical sketch, still the fundamental document for all biographical work on the man, is a most welcome expression of the steadily increasing interest in Rafinesque. In spite of displaying an overwhelming amount of travelling done and of interests developed by Rafinesque, this self-

description is still rather an understatement of the actual truth. The same is true of the almost unbelievable amount of ill luck and bad treatment experienced by the "eccentric naturalist." This autobiography, in listing carefully the scientific contacts of Rafinesque, which are identified by Dr. F. W. Pennell and Verdoorn in an excellent index, gives a lively picture of American science in the first half of the 19th century,—and of the state of things in Sicily between 1805 and 1815 where Rafinesque was confined during the blockade. As Constantine Samuel Rafinesque-Schmaltz was born in 1783 in Constantinople the son of a French merchant and a Greek lady of German ancestry, and as he was educated in France and Italy, allusions to other countries than the United States and Sicily, the two countries he studied longest and most intensely, are not lacking. Rafinesque is particularly important for medical historians because of his continued interest in medical botany and spas. His invention of a panacea for consumption should not be held too strongly against him. Here as in all his many inventions he was perfectly sincere. And as far as such panaceas go—this has happened even to still greater men in more recent times.

ERWIN H. ACKERKNECHT

CHARLES A. BROWNE. *Thomas Jefferson and the Scientific Trends of His Time.* Chronica Botanica, vol. 8, no. 3, pp. 363-424. Waltham, Mass.: the Chronica Botanica Co.; New York: G. E. Stechert and Co., 1944. Illustrated. $1.25.

Thomas Jefferson's interest in science is common knowledge and has received ample attention from many points of view, as a glimpse at the bibliography at the end of the present booklet shows. The author presents an outline of Jefferson's interests and activities in the various branches of science, underlining his utilitarian approach and his cautious attitude where radical new theories were propounded, as, for instance, Lavoisier's reform of chemical nomenclature. By quoting copiously from Jefferson's writings, particularly his letters, Dr. Browne has also elucidated his relationship to the ideas of many outstanding contemporary scientists such as Ingen-Houz and Priestley. Although a friend of Benjamin Rush, a propagator of vaccination, and appreciative of anatomy and surgery, Jefferson apparently trusted in the vis medicatrix naturae rather than in the medical theories and practices of his days.

In a booklet, the title of which emphasizes Jefferson's relationship to the scientific trends of his time, one might perhaps have wished to find a more searching discussion of the philosophical attitudes which shaped scientific ideas in the late 18th and early 19th century. However, as it is, the essay gives an interesting and convenient survey of Jefferson's scientific thoughts and enterprises, of particular value to those who wish to be introduced to the subject.

O. TEMKIN

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